

10/609,298

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| | | | |
|------|----|--------|---|
| NEWS | 1 | | Web Page for STN Seminar Schedule - N. America |
| NEWS | 2 | JAN 02 | STN pricing information for 2008 now available |
| NEWS | 3 | JAN 16 | CAS patent coverage enhanced to include exemplified prophetic substances |
| NEWS | 4 | JAN 28 | USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats |
| NEWS | 5 | JAN 28 | MARPAT searching enhanced |
| NEWS | 6 | JAN 28 | USGENE now provides USPTO sequence data within 3 days of publication |
| NEWS | 7 | JAN 28 | TOXCENTER enhanced with reloaded MEDLINE segment |
| NEWS | 8 | JAN 28 | MEDLINE and LMEDLINE reloaded with enhancements |
| NEWS | 9 | FEB 08 | STN Express, Version 8.3, now available |
| NEWS | 10 | FEB 20 | PCI now available as a replacement to DPCI |
| NEWS | 11 | FEB 25 | IFIREF reloaded with enhancements |
| NEWS | 12 | FEB 25 | IMSPRODUCT reloaded with enhancements |
| NEWS | 13 | FEB 29 | WPINDEX/WPIDS/WPIX enhanced with ECLA and current U.S. National Patent Classification |
| NEWS | 14 | MAR 31 | IFICDB, IFIPAT, and IFIUDB enhanced with new custom IPC display formats |
| NEWS | 15 | MAR 31 | CAS REGISTRY enhanced with additional experimental spectra |
| NEWS | 16 | MAR 31 | CA/CAplus and CASREACT patent number format for U.S. applications updated |
| NEWS | 17 | MAR 31 | LPCI now available as a replacement to LDPCI |
| NEWS | 18 | MAR 31 | EMBASE, EMBAL, and LEMBASE reloaded with enhancements |
| NEWS | 19 | APR 04 | STN AnaVist, Version 1, to be discontinued |
| NEWS | 20 | APR 15 | WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats |
| NEWS | 21 | APR 28 | EMBASE Controlled Term thesaurus enhanced |
| NEWS | 22 | APR 28 | IMSRESEARCH reloaded with enhancements |
| NEWS | 23 | MAY 30 | INPAFAMDB now available on STN for patent family searching |
| NEWS | 24 | MAY 30 | DGENE, PCTGEN, and USGENE enhanced with new homology sequence search option |
| NEWS | 25 | JUN 06 | EPFULL enhanced with 260,000 English abstracts |
| NEWS | 26 | JUN 06 | KOREPAT updated with 41,000 documents |

NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

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NEWS LOGIN Welcome Banner and News Items
NEWS IPC8 For general information regarding STN implementation of IPC 8

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FILE 'HOME' ENTERED AT 18:07:49 ON 08 JUN 2008

10/609,298

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=> file reg
COST IN U.S. DOLLARS          SINCE FILE      TOTAL
                                ENTRY        SESSION
FULL ESTIMATED COST          0.21          0.21
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FILE 'REGISTRY' ENTERED AT 18:07:59 ON 08 JUN 2008
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STRUCTURE FILE UPDATES: 6 JUN 2008 HIGHEST RN 1026208-38-7
DICTIONARY FILE UPDATES: 6 JUN 2008 HIGHEST RN 1026208-38-7

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```
=>
Uploading C:\Program Files\Stnexp\Queries\10609298a.str
```

L1 STRUCTURE uploaded

```
=> d l1
L1 HAS NO ANSWERS
L1      STR
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

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=> s l1
SAMPLE SEARCH INITIATED 18:08:35 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 2232 TO ITERATE

89.6% PROCESSED      2000 ITERATIONS          24 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01
```

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FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH    **COMPLETE**
PROJECTED ITERATIONS:   41806 TO    47474
PROJECTED ANSWERS:      225 TO     845
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L2 24 SEA SSS SAM L1

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FULL SEARCH INITIATED 18:08:41 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 44523 TO ITERATE
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100.0% PROCESSED     44523 ITERATIONS          519 ANSWERS
SEARCH TIME: 00.00.01
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L3 519 SEA SSS FUL L1

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=> file caplus
COST IN U.S. DOLLARS          SINCE FILE      TOTAL
                                ENTRY        SESSION
FULL ESTIMATED COST          178.36          178.57
```

McIntosh

FILE 'CAPLUS' ENTERED AT 18:08:46 ON 08 JUN 2008
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FILE COVERS 1907 - 8 Jun 2008 VOL 148 ISS 24
FILE LAST UPDATED: 6 Jun 2008 (20080606/ED)

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<http://www.cas.org/legal/infopolicy.html>

```
=> s l3
L4      120 L3

=> s l4 and flavivirus or pestivirus or flaviviridae or hcv or hepatitis c
    1747 FLAVIVIRUS
    864 FLAVIVIRUSES
    2025 FLAVIVIRUS
        (FLAVIVIRUS OR FLAVIVIRUSES)
    501 PESTIVIRUS
    266 PESTIVIRUSES
    597 PESTIVIRUS
        (PESTIVIRUS OR PESTIVIRUSES)
    645 FLAVIVIRIDAE
    14183 HCV
    24 HCVS
    14187 HCV
        (HCV OR HCVS)
    67218 HEPATITIS
    1 HEPATITISES
    67218 HEPATITIS
        (HEPATITIS OR HEPATITISES)
    3835463 C
    20967 HEPATITIS C
        (HEPATITIS(W)C)
L5      22498 L4 AND FLAVIVIRUS OR PESTIVIRUS OR FLAVIVIRIDAE OR HCV OR HEPATI
TIS C

=> s l4 and (flavivirus or pestivirus or flaviviridae or hcv or hepatitis c)
    1747 FLAVIVIRUS
    864 FLAVIVIRUSES
    2025 FLAVIVIRUS
        (FLAVIVIRUS OR FLAVIVIRUSES)
    501 PESTIVIRUS
    266 PESTIVIRUSES
    597 PESTIVIRUS
        (PESTIVIRUS OR PESTIVIRUSES)
    645 FLAVIVIRIDAE
    14183 HCV
    24 HCVS
    14187 HCV
        (HCV OR HCVS)
    67218 HEPATITIS
    1 HEPATITISES
    67218 HEPATITIS
        (HEPATITIS OR HEPATITISES)
    3835463 C
    20967 HEPATITIS C
        (HEPATITIS(W)C)
L6      58 L4 AND (FLAVIVIRUS OR PESTIVIRUS OR FLAVIVIRIDAE OR HCV OR HEPAT
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ITIS C)

=> d bib abs hitstr 40-58 16

L6 ANSWER 40 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2006:103884 CAPLUS
 DN 144:171198
 TI Preparation of alkyl-substituted 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs via condensation of the lactone to nucleosides as potential antiviral agents
 IN Wang, Peiyuan; Stec, Wojciech; Clark, Jeremy; Chun, Byoung-Kwon; Shi, Junxing; Du, Jinfa
 PA Pharmasset, Inc., USA
 SO PCT Int. Appl., 34 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|----------|
| PI WO 2006012440 | A2 | 20060202 | WO 2005-US25916 | 20050721 |
| WO 2006012440 | A3 | 20060727 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| AU 2005267051 | A1 | 20060202 | AU 2005-267051 | 20050721 |
| CA 2574651 | A1 | 20060202 | CA 2005-2574651 | 20050721 |
| EP 1773856 | A2 | 20070418 | EP 2005-775359 | 20050721 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | | |
| CN 101023094 | A | 20070822 | CN 2005-80031530 | 20050721 |
| BR 2005012104 | A | 20080311 | BR 2005-12104 | 20050721 |
| JP 2008507547 | T | 20080313 | JP 2007-522763 | 20050721 |
| US 20060199783 | A1 | 20060907 | US 2006-353597 | 20060213 |
| MX 200700803 | A | 20070402 | MX 2007-803 | 20070119 |
| IN 2007KN00605 | A | 20070706 | IN 2007-KN605 | 20070220 |
| KR 2007114344 | A | 20071203 | KR 2007-703980 | 20070220 |
| PRAI US 2004-589866P | P | 20040721 | | |
| US 2004-608320P | P | 20040909 | | |
| US 2005-185988 | A1 | 20050721 | | |
| WO 2005-US25916 | W | 20050721 | | |
| OS MARPAT 144:171198 | | | | |
| GI | | | | |

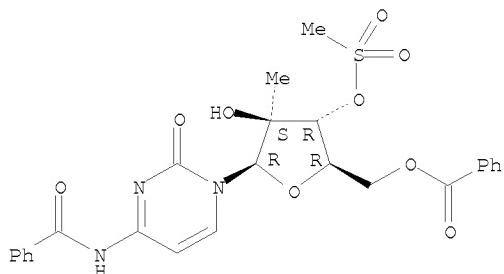
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A process for preparing of 2-deoxy-2-fluoro-2-methyl-D-ribonolactones, I, wherein R1 and R2 can independently be H, CH₃, acetyl, benzoyl, pivaloyl, 4-nitrobenzoyl, 3-nitrobenzoyl, 2-nitrobenzoyl, 4-chlorobenzoyl, 3-chlorobenzoyl, 2-chlorobenzoyl, 4-methylbenzoyl, 3-methylbenzoyl, 2-methylbenzoyl, 4-phenylbenzoyl, benzyl, 4-methoxybenzyl, trityl, trialkylsilyl, t-butyl-dialkylsilyl, t-butyldiphenylsilyl, TIPDS, THP, MOM, or MEM are prepared and used in the condensation to 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs. Thus, 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs II and III, wherein X is a halogen; Y is N or CH; Z is a halogen, hydroxyl, ether, thiol, thicether, (un)substituted amine or alkyl; R1' is alkyl, vinyl, ethynyl; R2' and R3' can be same or different H, alkyl, arylalkyl, acyl, cyclic acetal such as 2',3'-O-isopropylidene or 2',3-O-benzylidene, or 2',3'-cyclic carbonate; R4, R5, and R6 are independently H, halogen, hydroxyl, ether, thiol, thioether, N₃,

(un)substituted amine, (un)substituted amido, alkyl, halogenated alkyl, alkenyl, halogenated alkenyl, alkynyl, halogenated alkynyl, hydroxy alkyl, alkoxy are prepared and are potential anti-HCV agents. Specifically, IV was prepared (no yield, claimed) via condensation, alkylation and stereoselective fluorination reactions and can exhibit potential use as an anti-HCV agent.

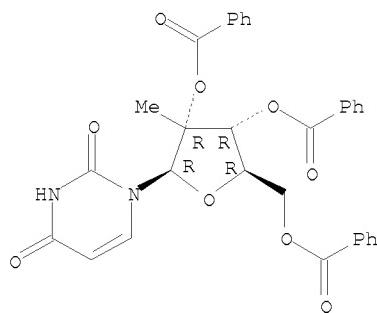
IT 874638-81-0P
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of alkyl-substituted 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs via condensation of the lactone to nucleosides)
 RN 874638-81-0 CAPLUS
 CN Benzamide, N-[1-[5-O-benzoyl-2-C-methyl-3-O-(methylsulfonyl)- β -D-arabinofuranosyl]-1,2-dihydro-2-oxo-4-pyrimidinyl]-(CA INDEX NAME)

Absolute stereochemistry.



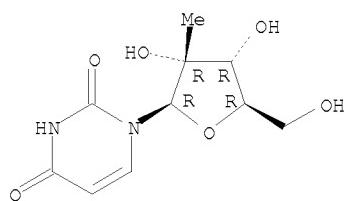
L6 ANSWER 41 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2005:1151389 CAPLUS
 DN 145:271979
 TI NM 283, an efficient prodrug of the potent anti-HCV agent 2'-C-methylcytidine
 AU Pierra, C.; Benzaria, S.; Amador, A.; Moussa, A.; Mathieu, S.; Storer, R.; Gosselin, G.
 CS Laboratoire Cooperatif Idenix, CNRS, Universite Montpellier II, Montpellier, 5, Fr.
 SO Nucleosides, Nucleotides & Nucleic Acids (2005), 24(5-7), 767-770
 CODEN: NNNAFY; ISSN: 1525-7770
 PB Taylor & Francis, Inc.
 DT Journal
 LA English
 OS CASREACT 145:271979
 AB In order to improve the oral bioavailability of 2'-C-methylcytidine, a potent anti-HCV agent, the corresponding 3'-O-L-valinyl ester derivative (NM 283) has been synthesized. Based on its ease of synthesis and its physicochem. properties, NM 283 has emerged as a promising antiviral drug for treatment of chronic HCV infection.
 IT 23643-36-9P 31448-54-1P 640725-70-8P
 642075-42-1P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of NM 283 as efficient prodrug of potent anti-HCV agent 2'-C-methylcytidine)
 RN 23643-36-9 CAPLUS
 CN 2,4(1H,3H)-Pyrimidinedione, 1-(2,3,5-tri-O-benzoyl-2-C-methyl- β -D-ribofuranosyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



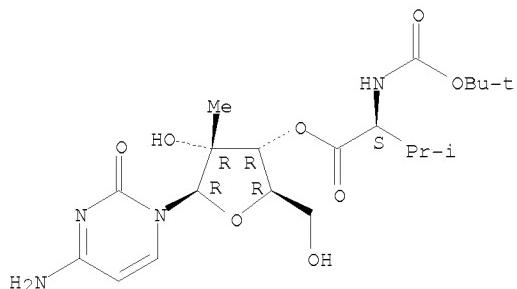
RN 31448-54-1 CAPLUS
 CN Uridine, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



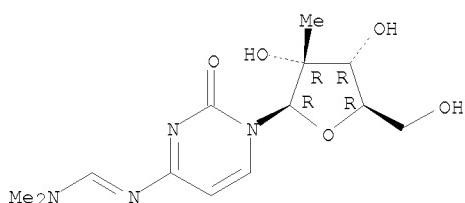
RN 640725-70-8 CAPLUS
 CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with
 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry.



RN 642075-42-1 CAPLUS
 CN Cytidine, N-[(dimethylamino)methylene]-2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry unknown.



IT 20724-73-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);

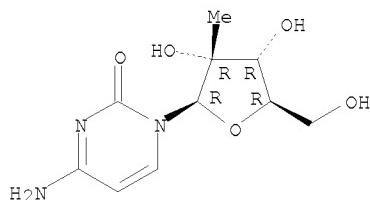
USES (Uses)

(preparation of NM 283 as efficient prodrug of potent anti-HCV agent 2'-C-methylcytidine)

RN 20724-73-6 CAPLUS

CN Cytidine, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



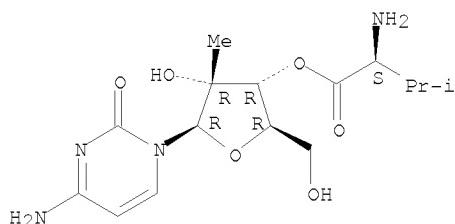
IT 640725-71-9P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prodrug; preparation of NM 283 as efficient prodrug of potent anti-HCV agent 2'-C-methylcytidine)

RN 640725-71-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



●2 HCl

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMATL6 ANSWER 42 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:684531 CAPLUS

DN 143:431740

TI Emerging drugs for chronic hepatitis C

AU Bhopale, Girish Mahadeorao; Nanda, Rabindra Kumar

CS Research and Development Division, Hindustan Antibiotics Limited, Pimpri, Pune, 411018, India

SO Hepatology Research (2005), 32(3), 146-153
CODEN: HPRSFM; ISSN: 1386-6346

PB Elsevier B.V.

DT Journal; General Review

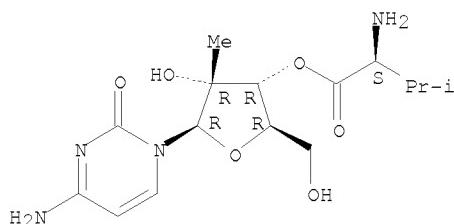
LA English

AB A review. Hepatitis C virus (HCV) is a major cause of chronic hepatitis, liver cirrhosis and hepatocellular carcinoma worldwide. A combination therapy comprising pegylated interferon and ribavirin currently represents the most effective therapy for chronic HCV infection. The limitations of this current therapy mainly its efficacy and significant side effects have prompted the development of new drugs. Few categories of therapeutic agents appear promising for future therapy, e.g. novel interferons, ribavirin analogs, antisense oligonucleotides, short interfering RNAs, ribozymes, enzyme inhibitors, immunomodulatory agents, antifibrotic agents, therapeutic vaccines and antibodies. Few drugs belong to afore-mentioned categories have already reached the different clinical phases of development. The

present article highlights the status of current available therapies and emerging drugs for the treatment of hepatitis C.

- IT 640725-71-9, NM 283
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (NM283 proved promising therapeutic effect in treating chronic hepatitis C patient)
- RN 640725-71-9 CAPLUS
- CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

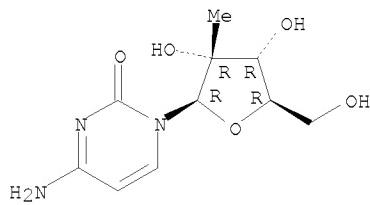


● 2 HCl

RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

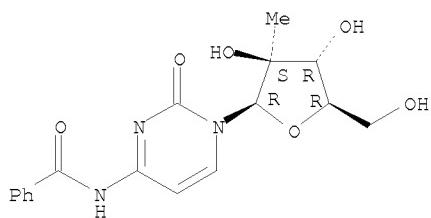
- L6 ANSWER 43 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2005:648160 CAPLUS
 DN 143:248607
 TI Design, Synthesis, and Antiviral Activity of 2'-Deoxy-2'-fluoro-2'-C-methyl-cytidine, a Potent Inhibitor of Hepatitis C Virus Replication
 AU Clark, Jeremy L.; Hollecker, Laurent; Mason, J. Christian; Stuyver, Lieven J.; Tharnish, Phillip M.; Lostia, Stefania; McBrayer, Tamara R.; Schinazi, Raymond F.; Watanabe, Kyoichi A.; Otto, Michael J.; Furman, Phillip A.; Stec, Wojciech J.; Patterson, Steven E.; Pankiewicz, Krzysztof W.
 CS Pharmasset, Inc., Princeton, NJ, 08540, USA
 SO Journal of Medicinal Chemistry (2005), 48(17), 5504-5508
 CODEN: JMCMAR; ISSN: 0022-2623
 PB American Chemical Society
 DT Journal
 LA English
 OS CASREACT 143:248607
 AB The pyrimidine nucleoside- β -D-2'-deoxy-2'-fluoro-2'-C-methylcytidine (I) was designed as a hepatitis C virus RNA-dependent RNA polymerase (HCV RdRp) inhibitor. The title compound was obtained by a DAST fluorination of N4-benzoyl-1-(2-methyl-3,5-di-O-benzoyl- β -D-arabinofuranosyl)cytosine to provide N4-benzoyl-1-(2-fluoro-2-methyl-3,5-di-O-benzoyl- β -D-ribofuranosyl)cytosine. The protected 2'-C-methylcytidine was obtained as a byproduct from the DAST fluorination and allowed for the preparation of two biol. active compds. from a common precursor. Compound I and 2'-C-methylcytidine were assayed in a sub-genomic HCV replicon assay system and found to be potent and selective inhibitors of HCV replication. Compd.I shows increased inhibitory activity in the HCV replicon assay compared to 2'-C-methylcytidine and low cellular toxicity.
 IT 20724-73-6
 RL: PAC (Pharmacological activity); BIOL (Biological study)
 (design, synthesis via fluorination, and antiviral activity of 2'-deoxy-2'-fluoro-2'-C-methyl-cytidine, a potent inhibitor of Hepatitis C virus replication)
 RN 20724-73-6 CAPLUS
 CN Cytidine, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



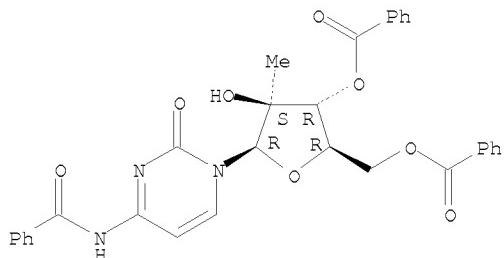
IT 817204-35-6P 863329-62-8P 863329-64-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (design, synthesis via fluorination, and antiviral activity of 2'-deoxy-2'-fluoro-2-C-methyl-cytidine, a potent inhibitor of Hepatitis C virus replication)
 RN 817204-35-6 CAPLUS
 CN Benzamide, N-[1,2-dihydro-1-(2-C-methyl-β-D-arabinofuranosyl)-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



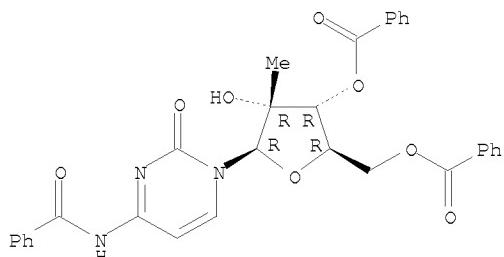
RN 863329-62-8 CAPLUS
 CN Benzamide, N-[1-(3,5-di-O-benzoyl-2-C-methyl-β-D-arabinofuranosyl)-1,2-dihydro-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 863329-64-0 CAPLUS
 CN Cytidine, N-benzoyl-2'-C-methyl-, 3',5'-dibenzoate (9CI) (CA INDEX NAME)

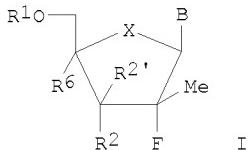
Absolute stereochemistry. Rotation (+).



RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 44 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2005:34765 CAPLUS
 DN 142:94074
 TI Preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleoside analogs as antiviral agents
 IN Clark, Jeremy
 PA Pharmasset, Ltd., Barbados
 SO PCT Int. Appl., 228 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--|------|----------|------------------|----------|
| PI | WO 2005003147 | A2 | 20050113 | WO 2004-US12472 | 20040421 |
| | WO 2005003147 | A3 | 20050303 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
TD, TG | | | | |
| | AU 2004253860 | A2 | 20050113 | AU 2004-253860 | 20040421 |
| | AU 2004253860 | A1 | 20050113 | | |
| | CA 2527657 | A1 | 20050113 | CA 2004-2527657 | 20040421 |
| | US 20050009737 | A1 | 20050113 | US 2004-828753 | 20040421 |
| | EP 1633766 | A2 | 20060315 | EP 2004-775900 | 20040421 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| | BR 2004010846 | A | 20060627 | BR 2004-10846 | 20040421 |
| | CN 1816558 | A | 20060809 | CN 2004-80019148 | 20040421 |
| | JP 2006526629 | T | 20061124 | JP 2006-513231 | 20040421 |
| | MX 2005PA12788 | A | 20060222 | MX 2005-PA12788 | 20051125 |
| | IN 2005DN06087 | A | 20080509 | IN 2005-DN6087 | 20051227 |
| | NO 2005006221 | A | 20051228 | NO 2005-6221 | 20051228 |
| | US 20080070861 | A1 | 20080320 | US 2007-854218 | 20070912 |
| PRAI | US 2003-474368P | P | 20030530 | | |
| | US 2004-828753 | A3 | 20040421 | | |
| | WO 2004-US12472 | W | 20040421 | | |
| OS | MARPAT 142:94074 | | | | |
| GI | | | | | |



AB The disclosed invention provides nucleoside analogs I, wherein B is purine and pyrimidine nucleobase; X is O, S, CH₂, Se, NH, N-alkyl, CH₂W, C(W)₂; W is F, Cl, Br, iodide; R1 is H, phosphate, H-phosphonate, acyl, Ph, alkyl, carboxyalkylamino, sulfonate ester, peptide, amino acid, sugar residue; R2 and R2' are independently H, alkyl, alkenyl, alkynyl, vinyl, N₃, CN, halogen, NO₂, ester, alkoxy, thioalkyl, sulfoxide, sulfonyl; R6 is alkyl, CN, Me, OMe, OEt, CH₂OH, CH₂F, N₃, CHCN, CH₂N₃, CH₂NH₂, CH₂NHMe, CH₂NMe₂, alkynyl; and methods of treating a Flaviviridae infection, including hepatitis C virus, West Nile Virus, yellow fever virus, and a rhinovirus infection in a host, including animals, and especially human, using a (2'R)-2'-deoxy-2'-fluoro-2'-C-Me nucleosides, or a pharmaceutically acceptable salt or prodrug thereof. Thus, (2'R)-2'-deoxy-2'-fluoro-2'-C-methylcytidine was prepared and tested as antiviral agent. The effects the nucleoside analogs tested on human bone

marrow cells are reported. ($2'R$)-2'-deoxy-2'-fluoro-2'-C-methylcytidine shows activity against Rhinovirus, West Nile virus, Yellow Fever virus, and Dengue virus. Cytotoxicity and effect of nucleoside analogs on human bone marrow cells are reported.

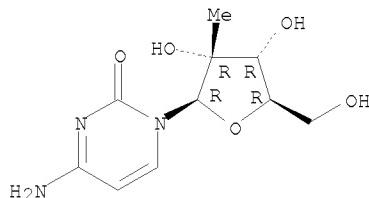
IT 20724-73-6 374750-28-4

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of modified fluorinated ($2'R$)-2'-deoxy-2'-fluoro-2'-C-Me nucleoside analogs as antiviral agents)

RN 20724-73-6 CAPLUS

CN Cytidine, 2'-C-methyl- (CA INDEX NAME)

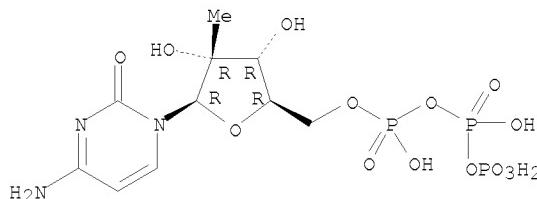
Absolute stereochemistry.



RN 374750-28-4 CAPLUS

CN Cytidine 5'-tetrahydrogen triphosphate, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



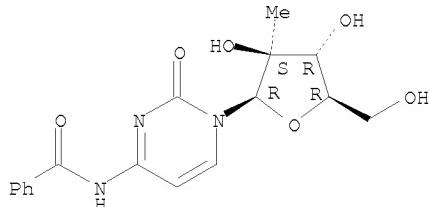
IT 817204-35-6P 817204-36-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of modified fluorinated ($2'R$)-2'-deoxy-2'-fluoro-2'-C-Me nucleoside analogs as antiviral agents)

RN 817204-35-6 CAPLUS

CN Benzamide, N-[1,2-dihydro-1-(2-C-methyl- β -D-arabinofuranosyl)-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

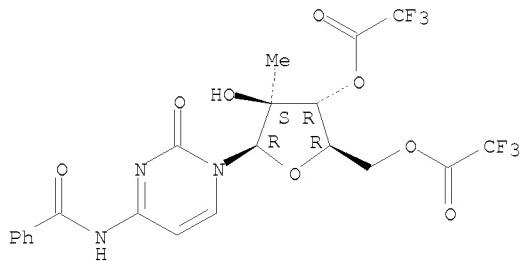
Absolute stereochemistry. Rotation (+).



RN 817204-36-7 CAPLUS

CN Benzamide, N-[1,2-dihydro-1-[2-C-methyl-3,5-bis-O-(trifluoroacetyl)- β -D-arabinofuranosyl]-2-oxo-4-pyrimidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 45 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2004:817630 CAPLUS

DN 141:307495

TI Use of nucleoside compounds and PALA for the treatment of flaviviridae infections

IN Stuyver, Lieven J.

PA Pharmasset Ltd., Barbados

SO PCT Int. Appl., 120 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|------------------|----------|
| PI | WO 2004084796 | A2 | 20041007 | WO 2004-IB1429 | 20040329 |
| | WO 2004084796 | A3 | 20060406 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
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| | AU 2004224575 | A1 | 20041007 | AU 2004-224575 | 20040329 |
| | CA 2529311 | A1 | 20041007 | CA 2004-2529311 | 20040329 |
| | US 20050049204 | A1 | 20050303 | US 2004-812448 | 20040329 |
| | EP 1626692 | A2 | 20060222 | EP 2004-724085 | 20040329 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK | | | | |
| | BR 2004008846 | A | 20060704 | BR 2004-8846 | 20040329 |
| | JP 2006524227 | T | 20061026 | JP 2006-506588 | 20040329 |
| | CN 1980678 | A | 20070613 | CN 2004-80011746 | 20040329 |
| | MX 2005PA10419 | A | 20060531 | MX 2005-PA10419 | 20050928 |
| PRAI | US 2003-458635P | P | 20030328 | | |
| | WO 2004-IB1429 | W | 20040329 | | |

OS MARPAT 141:307495

AB The invention discloses a composition for and a method of treating Flaviviridae infections, e.g. bovine viral diarrhea virus, dengue Virus, West Nile virus, and hepatitis C virus, as well as abnormal cellular proliferation, in a host, including animals, and especially humans, using a nucleoside compound (Markush included) or N-(phosphonoacetyl)-L-aspartate (PALA), or a pharmaceutically acceptable salt or prodrug thereof.

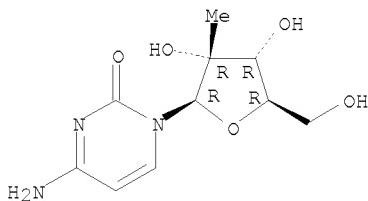
IT 20724-73-6

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (nucleoside compds. and PALA for treatment of flaviviridae infections)

RN 20724-73-6 CAPLUS

Cytidine, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 46 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2004:780543 CAPLUS

DN 141:296247

TI Preparation of cytidine nucleoside analogs as antiviral agents
 IN Girardet, Jean-Luc; Koh, Yung-Hyo; An, Haoyun; Hong, Zhi

PA Ribapharm Inc., USA

SO PCT Int. Appl., 59 pp.

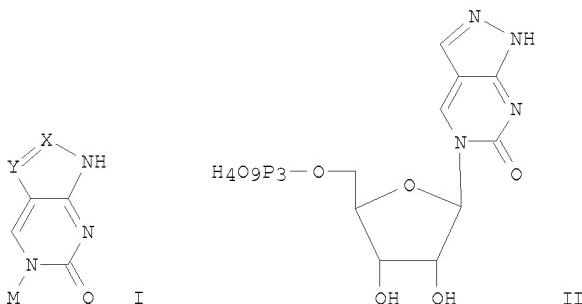
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2004080466 | A1 | 20040923 | WO 2003-US6992 | 20030307 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | AU 2003225705 | A1 | 20040930 | AU 2003-225705 | 20030307 |
| PRAI | WO 2003-US6992 | A | 20030307 | | |
| OS | MARPAT 141:296247 | | | | |
| GI | | | | | |



AB Cytidine analogs I, wherein -X=Y- is -N=N-, -CH=N-, -N=CZ- or -CH=CZ-, wherein Z is H, halogen, or alkyl, and wherein M is a sugar or sugar analog; wherein the compound has a D-configuration or an L-configuration; with the proviso that where M is a substituted sugar with a ribofuranose ring having a heteroatom and substituents R1 and R2 on the C3'-atom, R3 and R4 on the C2'-atom, and R5 on the C5'-atom, R1-R4 together are not independently H, OH, F, NH2, N3, O-hydrocarbyl, or a reporter moiety, when the heteroatom is O, S, Se, SO, N-alkyl, or CH2, and when R5 is OH, SH, NH2, monophosphate, diphosphate, triphosphate, thiophosphate, or boranophosphate; and with the further proviso that M does not comprise a cyclopropenyl group, a morpholino group, or M is not a phosphonylmethoxyethyl, their prodrugs and/or metabolites are employed as pharmaceutically active compds. for treatment of diseases responsive to such compds. Particularly preferred diseases include viral diseases (e.g., HCV infection) and neoplasms (no biol. data). Thus

nucleoside analog II was prepared and tested as antiviral agent. The virus is an HCV virus, an HIV virus, an RSV virus, an influenza virus, or a an HBV virus.

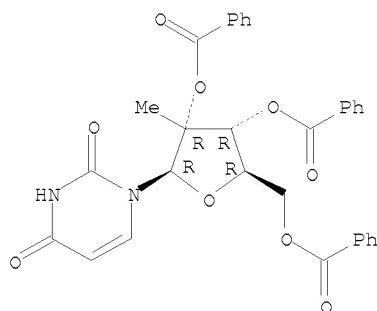
IT 23643-36-9

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of cytidine nucleoside analogs as antiviral agents)

RN 23643-36-9 CAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-(2,3,5-tri-O-benzoyl-2-C-methyl- β -D-ribofuranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 760965-52-4P 760965-53-5P 760965-55-7P

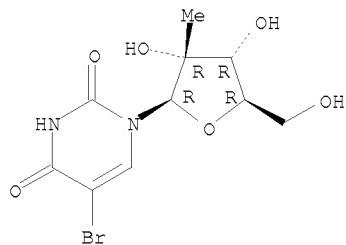
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation of cytidine nucleoside analogs as antiviral agents)

RN 760965-52-4 CAPLUS

CN Uridine, 5-bromo-2'-C-methyl- (9CI) (CA INDEX NAME)

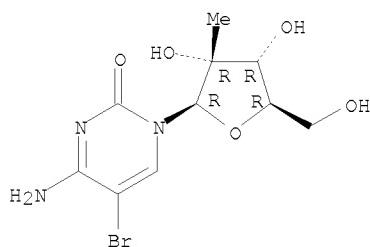
Absolute stereochemistry.



RN 760965-53-5 CAPLUS

CN Cytidine, 5-bromo-2'-C-methyl- (9CI) (CA INDEX NAME)

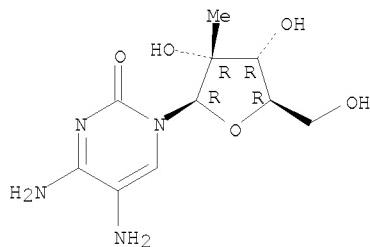
Absolute stereochemistry.



RN 760965-55-7 CAPLUS

CN Cytidine, 5-amino-2'-C-methyl- (9CI) (CA INDEX NAME)

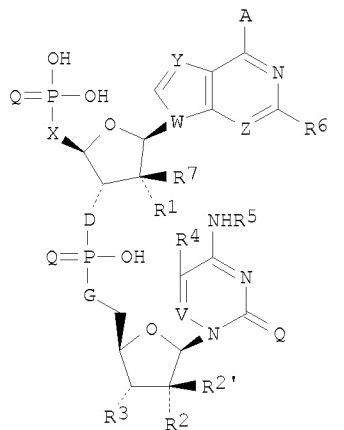
Absolute stereochemistry.



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 47 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:652668 CAPLUS
DN 141:167739
TI Diribonucleotides as specific viral RNA-polymerase inhibitors for the treatment or prevention of viral infections
IN Wu, Jim Zhen; An, Haoyun; Hong, Zhi
PA USA
SO U.S. Pat. Appl. Publ., 12 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

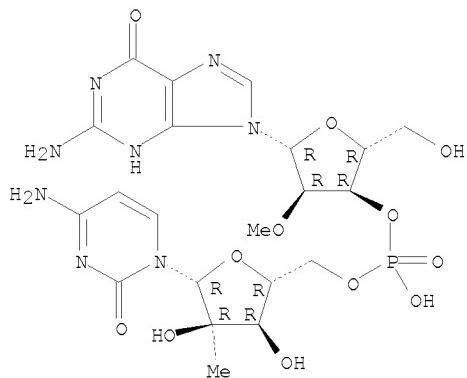
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| PI US 20040158054 | A1 | 20040812 | US 2003-360218 | 20030207 |
| PRAI US 2003-360218 | | | 20030207 | |
| OS MARPAT 141:167739 | | | | |
| GI | | | | |



AB The invention discloses compds. and methods using dinucleotide compds. I (A = H, OR, SR, NH₂, or NHR; Q = O or S; V, W, Y, and Z = CH or N; X = O, S, NR, etc.; D and G = null, CH₂, O, etc.; R₁, R₂, R_{2'}, R₃ = H, OR, halogen, CF₃ etc.; R₄ = R; R₅ = H, NH₂, NHR, etc.; R₆ = H, NH₂, NHCO_R, etc.; R₇ = H, OR, SR, halogen, etc.; R = H, (un)substituted alkyl, aryl, etc.) comprising a first and second nucleoside. The dinucleotide inhibits viral RNA polymerase and at least one of the nucleosides exhibits antiviral activity when cleaved from the dinucleotide.
IT 735268-87-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (diribonucleotides as specific viral RNA-polymerase inhibitors for treatment or prevention of viral infections)
RN 735268-87-8 CAPLUS

CN Cytidine, 2'-O-methylguanylyl-(3'→5')-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 735268-88-9

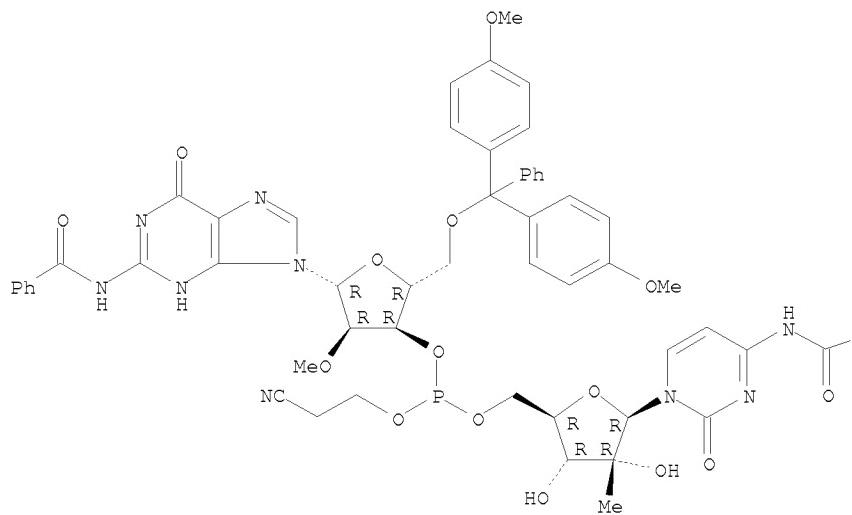
RL: RCT (Reactant); RACT (Reactant or reagent)
(diribonucleotides as specific viral RNA-polymerase inhibitors for treatment or prevention of viral infections)

RN 735268-88-9 CAPLUS

CN Cytidine, N-benzoyl-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P(O)-(2-cyanoethyl)-P-dexo-2'-O-methylguanylyl-(3'→5')-N-benzoyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

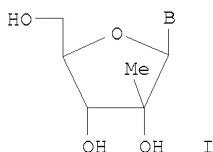
PAGE 1-A



Ph

L6 ANSWER 48 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2004:566635 CAPLUS
 DN 141:89323
 TI Process for the production of 3'-nucleoside prodrugs
 IN Storer, Richard; Moussa, Adel; Mathieu, Steven; Qu, Lin
 PA Idenix Cayman Limited, Cayman I.
 SO PCT Int. Appl., 57 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|----------|
| PI WO 2004058792 | A1 | 20040715 | WO 2003-US41603 | 20031223 |
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GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO,
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TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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| CA 2511616 | A1 | 20040715 | CA 2003-2511616 | 20031223 |
| AU 2003300434 | A1 | 20040722 | AU 2003-300434 | 20031223 |
| US 20040181051 | A1 | 20040916 | US 2003-746395 | 20031223 |
| EP 1575971 | A1 | 20050921 | EP 2003-814400 | 20031223 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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| BR 2003016868 | A | 20051025 | BR 2003-16868 | 20031223 |
| CN 1751058 | A | 20060322 | CN 2003-80109820 | 20031223 |
| JP 2006514038 | T | 20060427 | JP 2004-562599 | 20031223 |
| NZ 540913 | A | 20080229 | NZ 2003-540913 | 20031223 |
| ZA 2005005040 | A | 20060426 | ZA 2005-5040 | 20050621 |
| NO 2005003557 | A | 20050908 | NO 2005-3557 | 20050720 |
| PRAI US 2002-436150P | P | 20021223 | | |
| WO 2003-US41603 | W | 20031223 | | |
| OS CASREACT 141:89323; MARPAT 141:89323 | | | | |
| GI | | | | |



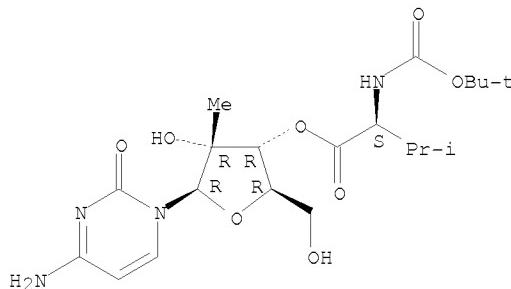
AB Provided is a single-step process for the regioselective 3'-acylation of a ribofuranosyl 2'- or 3'-branched nucleosides I, wherein B is nucleobase. These compds. are useful as antiviral agents, and in particular, can be used to treat Flaviviridae infections in a host in need thereof (no data). Thus, 9-(2'-C-methyl-3'-O-valinoyl- β -D-ribofuranosyl)-6-N-methyladenine dihydrochloride was prepared via regioselective esterification of 9-(2'-C-methyl- β -D-ribofuranosyl)-6-N-methyladenine with N-(tert-butoxycarbonyl)-L-valine.

IT 640725-70-8P
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
 (process for production of nucleoside prodrugs via regioselective esterification)

RN 640725-70-8 CAPLUS

CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry.

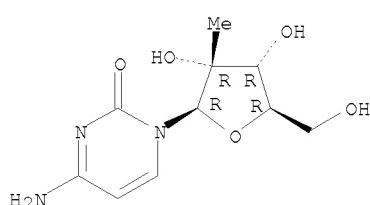


IT 20724-73-6
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (process for production of nucleoside prodrugs via regioselective esterification)

RN 20724-73-6 CAPLUS

CN Cytidine, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 49 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2004:453348 CAPLUS

DN 141:17578

TI Treatment of Flaviviridae infection with 2'-branched nucleosides and another mutation-inducing drug such as interferon

IN Sommadossi, Jean-Pierre; La Colla, Paolo; Standring, David; Bichko, Vadim; Qu, Lin

PA Idenix (Cayman) Limited, Cayman I.; Universita Degli Studi Di Cagliari
 SO PCT Int. Appl., 166 pp.
 CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------|------|----------|-----------------|----------|
| ----- | ---- | ----- | ----- | ----- |
| PI WO 2004046331 | A2 | 20040603 | WO 2003-US36714 | 20031117 |
| WO 2004046331 | A3 | 20060302 | | |

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 OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
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 CA 2506129 A1 20040603 CA 2003-2506129 20031117
 AU 2003298658 A1 20040615 AU 2003-298658 20031117
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 BR 2003016363 A 20051004 BR 2003-16363 20031117
 JP 2006519753 T 20060831 JP 2004-553823 20031117
 CN 1849142 A 20061018 CN 2003-80108747 20031117
 MX 2005PA05192 A 20050908 MX 2005-PA5192 20050513
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 PRAI US 2002-426675P P 20021115
 WO 2003-US36714 W 20031117

OS MARPAT 141:17578

AB The present invention discloses a method for the treatment of Flaviviridae infection that includes the administration of a 2'-branched nucleoside, or a pharmaceutically acceptable prodrug and/or salt thereof, to a human in need of therapy in combination or alternation with a drug that directly or indirectly induces a mutation in the viral genome at a location other than a mutation of a nucleotide that results in a change from serine to a different amino acid in the highly conserved consensus sequence, $\text{XRX}^{\text{u}}\text{S}^{\text{u}}$ GXXXT , of domain B of the RNA polymerase region, or is associated with such a mutation. The invention also includes a method to detect a mutant strain of Flaviviridae and a method for its treatment. Thus, in bovine viral diarrhea virus (BVDV)-infected MDBK cells treated with β -D-2'-methylcytidine, viruses resistant to the nucleoside appeared. The drug resistance was associated with a mutation in the NS5B gene which resulted in an S405T substitution in the encoded RNA-dependent RNA polymerase. These mutant viruses were sensitive to Intron A (interferon α -2b). Intron A and β -D-2'-methylcytidine exhibited synergistic inhibitory activity on BVDV growth in MDBK cells.

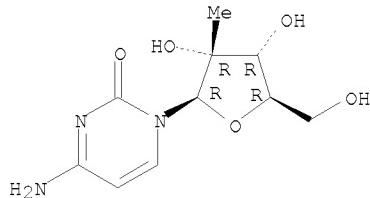
IT 20724-73-6

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (treatment of Flaviviridae infection with 2'-branched nucleosides and another mutation-inducing drug such as interferon)

RN 20724-73-6 CAPLUS

CN Cytidine, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



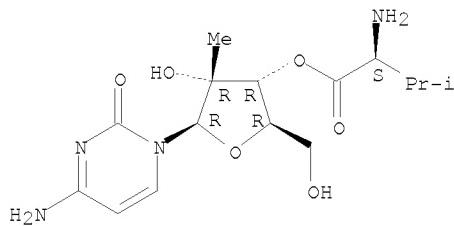
IT 640281-90-9

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (treatment of Flaviviridae infection with 2'-branched nucleosides and another mutation-inducing drug such as interferon)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L6 ANSWER 50 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:20697 CAPLUS
DN 140:87662
TI 2'- and 3'-nucleoside prodrugs for treating Flaviviridae infections
IN Sommadossi, Jean-pierre; La Colla, Paolo; Storer, Richard; Gosselin, Gilles
PA Idenix (Cayman) Limited, Cayman I.; Centre National de la Recherche Scientifique; Universita Degli Studi di Cagliari
SO PCT Int. Appl., 2498 pp.
CODEN: PIXXD2

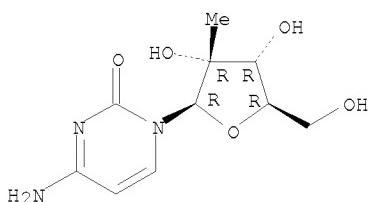
DT Patent
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FAN.CNT 4

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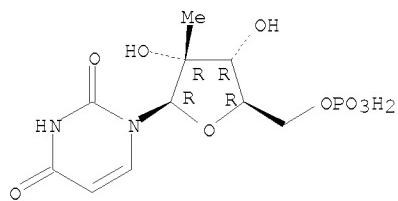
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| | US 2002-392351P | P | 20020628 | | |
| | US 2003-466194P | P | 20030428 | | |
| | US 2003-470949P | P | 20030514 | | |
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| US | 2003-608907 | A1 | 20030627 | | |
| US | 2003-609298 | A1 | 20030627 | | |
| WO | 2003-IB3901 | W | 20030627 | | |
| WO | 2004-US15395 | W | 20040514 | | |
| OS | MARPAT 140:87662 | | | | |
| AB | 2' And 3'-Prodrugs of 1', 2', 3', or 4'-branched β -D or β -L nucleosides, or their pharmaceutically acceptable salts and derivs., are described which are useful in the prevention and treatment of Flaviviridae infections and other related conditions. These modified nucleosides provide superior results against flaviviruses and pestiviruses, including hepatitis C virus and viruses generally that replicate through an RNA-dependent RNA reverse transcriptase. Compds., compns., methods and uses are provided for the treatment of Flaviviridae infection, including HCV infection, that include the administration of an effective amount of the prodrugs of the invention, or their pharmaceutically acceptable salts or derivs. These drugs may optionally be administered in combination or alternation with further antiviral agents to prevent or treat Flaviviridae infections and other related conditions. Preparation of compds. of the invention is included. | | | | |
| IT | 20724-73-6P | | | | |
| | RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (nucleoside prodrugs for treating Flaviviridae infections) | | | | |
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| CN | Cytidine, 2'-C-methyl- | (CA INDEX NAME) | | | |

Absolute stereochemistry.



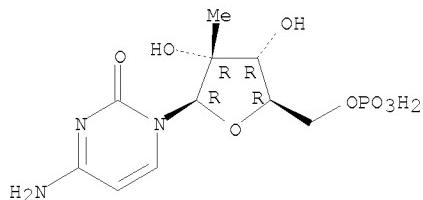
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| | RL: BSU (Biological study, unclassified); BIOL (Biological study) (nucleoside prodrugs for treating Flaviviridae infections) | |
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| CN | 5'-Uridylic acid, 2'-C-methyl- | (CA INDEX NAME) |

Absolute stereochemistry.



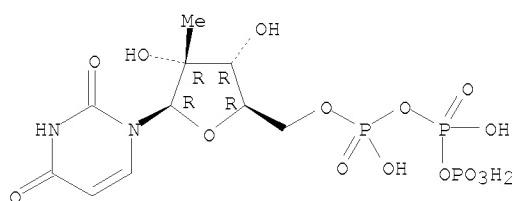
RN 386213-38-3 CAPLUS
CN 5'-Cytidylic acid, 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



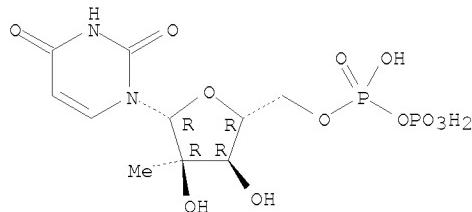
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BIOL (Biological study)
(nucleoside prodrugs for treating Flaviviridae infections)
RN 125911-76-4 CAPLUS
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Absolute stereochemistry.



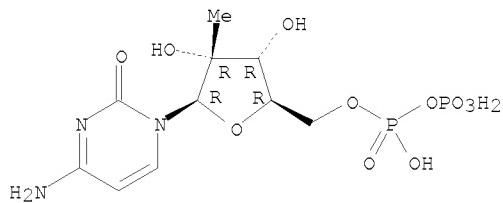
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CN Uridine 5'-(trihydrogen diphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



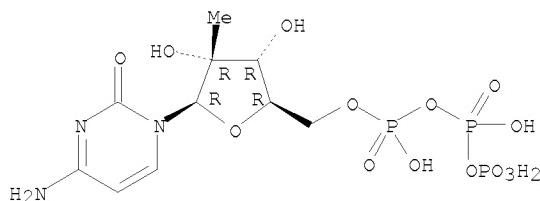
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CN Cytidine 5'-(trihydrogen diphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



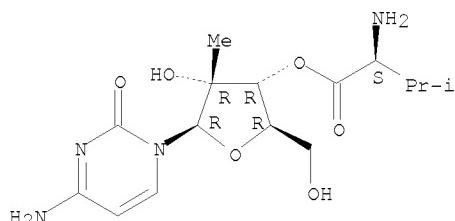
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 (nucleoside prodrugs for treating Flaviviridae infections)
 RN 374750-28-4 CAPLUS
 CN Cytidine 5'-triphosphate, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



IT 640725-71-9P
 RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (nucleoside prodrugs for treating Flaviviridae infections)
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 CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

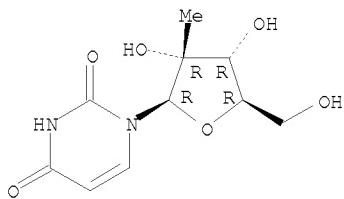
Absolute stereochemistry. Rotation (+).



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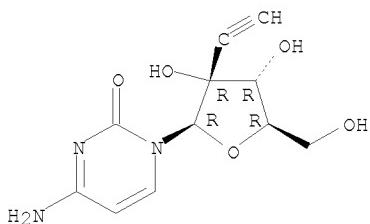
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 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
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 RN 31448-54-1 CAPLUS
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Absolute stereochemistry. Rotation (+).



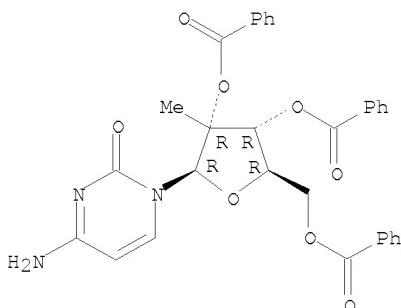
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Absolute stereochemistry.



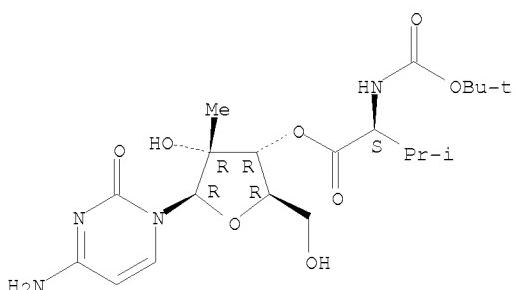
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Absolute stereochemistry.



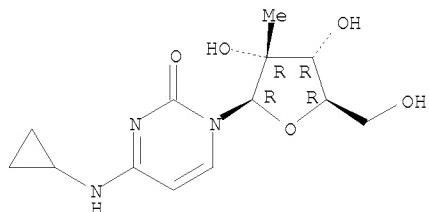
RN 640725-70-8 CAPLUS
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Absolute stereochemistry.



IT 622381-09-3
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (nucleoside prodrugs for treating Flaviviridae infections,
 and use with other agents)
 RN 622381-09-3 CAPLUS
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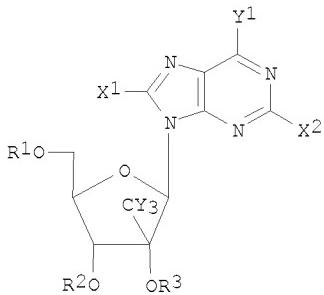
Absolute stereochemistry.



L6 ANSWER 51 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2004:20696 CAPLUS
 DN 140:77365
 TI Preparation of modified 2'- and 3'-nucleoside prodrugs for treating Flaviviridae infections
 IN Sommadossi, Jean-pierre; La Colla, Poalo; Storer, Richard; Gosselin, Gilles
 PA Idenix (Cayman) Limited, Cayman I.; Universita degli studi di Cagliari; Centre National de la Recherche Scientifique
 SO PCT Int. Appl., 201 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 4

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| PI | WO 2004002999 | A2 | 20040108 | WO 2003-IB3246 | 20030627 |
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| GI | | | | |

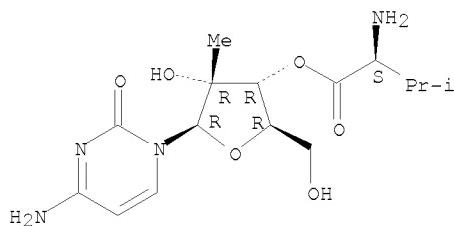


AB 2' And/or 3' prodrugs of 1', 2', 3' or 4'-branched-nucleosides I, wherein R1-R3 are independently H, phosphate, alkyl, acyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, CO-aryloxyalkyl, CO-substituted aryl, sulfonate ester, benzyl, wherein the Ph group is optionally substituted with one or more substituents, alkylsulfonyl, arylsulfonyl, aralkylsulfonyl, lipid, amino acid, carbohydrate, peptide, cholesterol; Y1 is hydrogen, bromo, chloro, fluoro, iodo, CN, OH, OR4, NH2, NHR4, NR4R5, SH or SR4; X1 and X2 are independently alkyl, CH3, CF3, CY3, 2-Br-Et, CH2F, CH2Cl, CH2CF3, CF2CF3, CY2CY3, CH2OH, alkenyl, alkynyl, COOH, COOR4, COO-alkyl, COO-aryl, CO-O-alkoxyalkyl, CONH2, CONHR4, CON(R4)2, halo, CN, N3, OH, CR4, NH2, NHR4, NR4R5, SH or SR5; Y is independently H, halo; and each R4 and R5 is independently hydrogen, acyl, alkyl, lower alkyl, alkenyl, alkynyl or cycloalkyl, and their pharmaceutically acceptable salts and derivs. are described. These prodrugs are useful in the prevention and treatment of Flaviviridae infections, including HCV infection, and other related conditions. Compds. and compns. of the prodrugs of the

present invention are described. Methods and uses are also provided that include the administration of an effective amount of the prodrugs of the present invention, or their pharmaceutically acceptable salts or derivs. These drugs may optionally be administered in combination or alteration with further anti-viral agents to prevent or treat Flaviviridae infections and other related conditions. Thus, antiviral activity of β -D-2'-C-methyl-7-methyl-6-phenyl-3,3a,5,8a-tetrahydro-1,3,4,5,7a-penta-aza-s-indacen-8-one is reported.

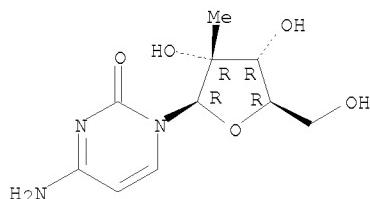
IT 640281-90-9P
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of modified and nucleoside prodrugs for treating flaviviridae infections)
 RN 640281-90-9 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 20724-73-6
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of modified and nucleoside prodrugs for treating flaviviridae infections)
 RN 20724-73-6 CAPLUS
 CN Cytidine, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 52 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2004:20443 CAPLUS
 DN 140:70984
 TI 2'-C-methyl-3'-O-L-valine ester ribofuranosyl cytidine for treatment of flaviviridae infections
 IN Sommadossi, Jean-Pierre; La Colla, Paolo
 PA Idenix (Cayman) Limited, Cayman I.; Universita Degli Studi di Cagliari
 SO PCT Int. Appl., 110 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 4

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| ----- | ---- | ----- | ----- | ----- |
| PI WO 2004002422 | A2 | 20040108 | WO 2003-US20431 | 20030627 |
| WO 2004002422 | A3 | 20050407 | | |
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CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR,
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 CA 2489552 A1 20040108 CA 2003-2489552 20030627
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 US 20070027065 A1 20070201 US 2004-5468 20041206
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 NO 2005000490 A 20050127 NO 2005-490 20050127
 US 20070275883 A1 20071129 US 2006-516928 20060906
 IN 2007DN08806 A 20080111 IN 2007-DN8806 20071115
 PRAI US 2002-392351P P 20020628
 US 2003-466194P P 20030428
 US 2003-470949P P 20030514
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 CN 2003-820501 A3 20030627
 CN 2003-820701 A3 20030627
 US 2003-607909 A1 20030627
 US 2003-608907 A1 20030627
 US 2003-609298 A1 20030627
 WO 2003-US20431 W 20030627
 WO 2004-US15395 W 20040514
 IN 2005-DN344 A3 20050128
 OS MARPAT 140:70984
 AB The 3'-L-valine ester of β -D-2'-C-methyl-ribofuranosyl cytidine provides superior results against flaviviruses and pestiviruses, including hepatitis C virus. Based on this discovery, compds., compns., methods and uses are provided for the treatment of flaviviridae, including HCV, that include the administration of an effective amount of val-mCyd or its salt,

ester, prodrug or derivative, optionally in a pharmaceutically acceptable carrier. In an alternative embodiment, val-mCyd is used to treat any virus that replicates through an RNA-dependent RNA polymerase. Several examples are provided of the pharmacol., mechanism of action, metabolism, side effects, and clin. efficacy of the title compound

IT 640281-90-9D, salts 642075-50-1 642075-51-2

642075-52-3 642075-53-4 642075-54-5

642075-55-6 642075-56-7 642075-57-8

642075-58-9 642075-59-0 642075-60-3

642075-61-4 642075-62-5 642075-63-6

642075-64-7 642075-65-8 642075-66-9

642075-67-0 642075-68-1 642075-69-2

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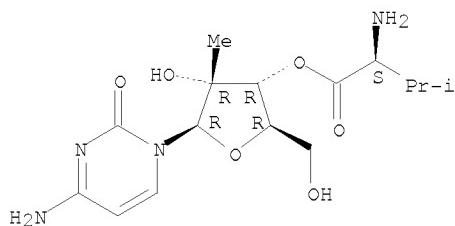
642075-77-2

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ribofuranosylcytidine methylvaline ester combined with other
antivirals for treatment of flaviviridae infections)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 642075-50-1 CAPLUS

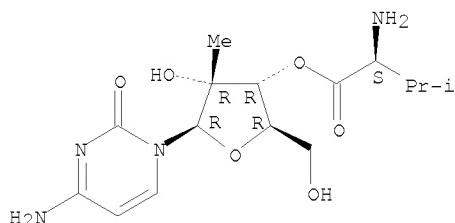
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 4-methylbenzenesulfonate
(salt) (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

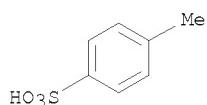
Absolute stereochemistry. Rotation (+).



CM 2

CRN 104-15-4

CMF C7 H8 O3 S



RN 642075-51-2 CAPLUS

McIntosh

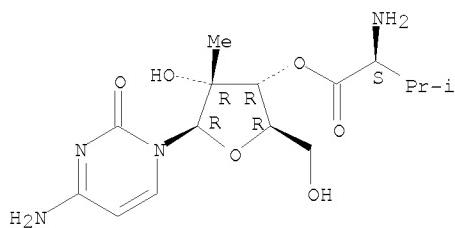
10/609,298

CN L-Valine, 3'-ester with 2'-C-methylcytidine, methanesulfonate (salt) (9CI)
(CA INDEX NAME)

CM 1

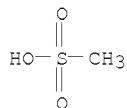
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 75-75-2
CMF C H4 O3 S

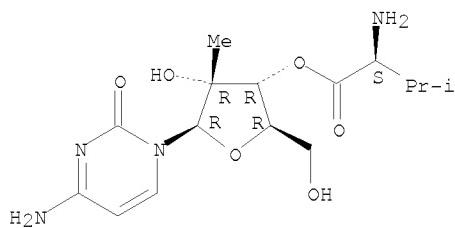


RN 642075-52-3 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, acetate (salt) (9CI) (CA INDEX NAME)

CM 1

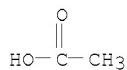
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 64-19-7
CMF C2 H4 O2



RN 642075-53-4 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-hydroxy-1,2,3-

McIntosh

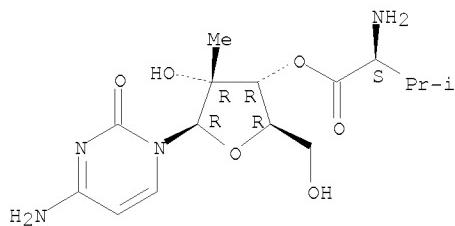
10/609,298

propanetricarboxylate (salt) (9CI) (CA INDEX NAME)

CM 1

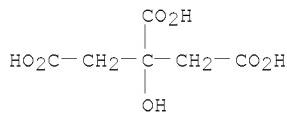
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 77-92-9
CMF C6 H8 O7

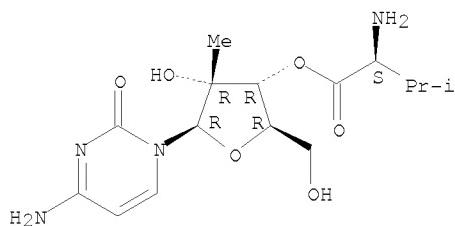


RN 642075-54-5 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, propanedioate (salt) (9CI)
(CA INDEX NAME)

CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 141-82-2
CMF C3 H4 O4

HO2C-CH2-CO2H

RN 642075-55-6 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, (2R,3R)-2,3-dihydroxybutanedioate (salt) (9CI) (CA INDEX NAME)

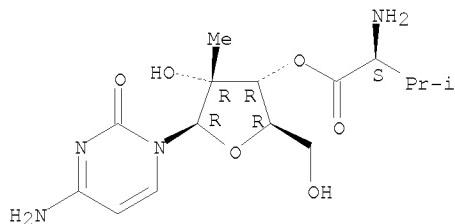
CM 1

McIntosh

10/609, 298

CRN 640281-90-9
CMF C15 H24 N4 O6

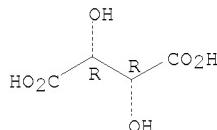
Absolute stereochemistry. Rotation (+).



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

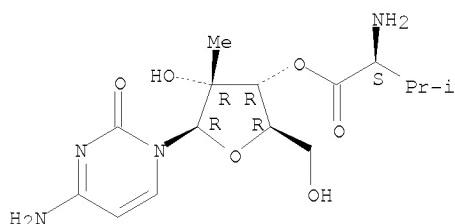


RN 642075-56-7 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, butanedioate (salt) (9CI)
(CA INDEX NAME)

CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-15-6
CMF C4 H6 O4

HO₂C-CH₂-CH₂-CO₂H

RN 642075-57-8 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, benzoate (salt) (9CI) (CA INDEX NAME)

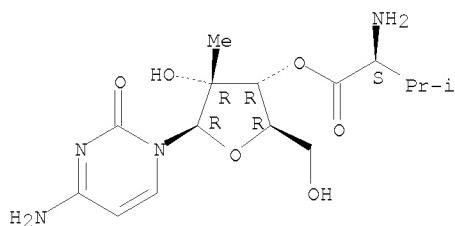
CM 1

McIntosh

10/609, 298

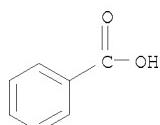
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 65-85-0
CMF C7 H6 O2

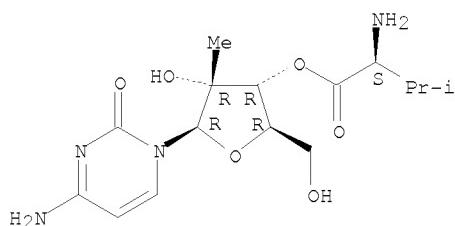


RN 642075-58-9 CAPLUS
CN L-Ascorbic acid, compd. with L-valine 3'-ester with 2'-C-methylcytidine
(9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

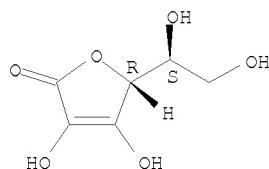
Absolute stereochemistry. Rotation (+).



CM 2

CRN 50-81-7
CMF C6 H8 O6

Absolute stereochemistry.



RN 642075-59-0 CAPLUS

McIntosh

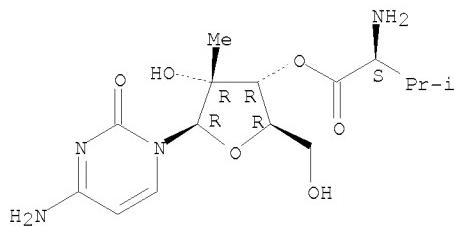
10/609,298

CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-oxopentanedioate (salt)
(9CI) (CA INDEX NAME)

CM 1

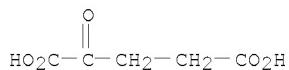
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 328-50-7
CMF C5 H6 O5

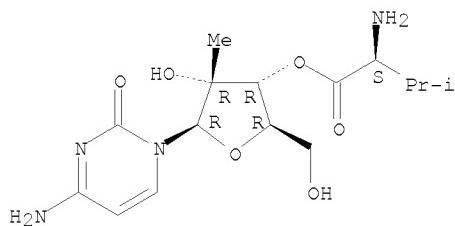


RN 642075-60-3 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2,3-dihydroxypropyl phosphate
(salt) (9CI) (CA INDEX NAME)

CM 1

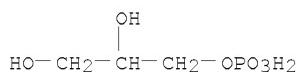
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 57-03-4
CMF C3 H9 O6 P



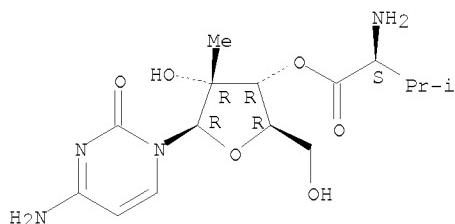
RN 642075-61-4 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, formate (salt) (9CI) (CA
INDEX NAME)

10/609, 298

CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 64-18-6
CMF C H2 O2

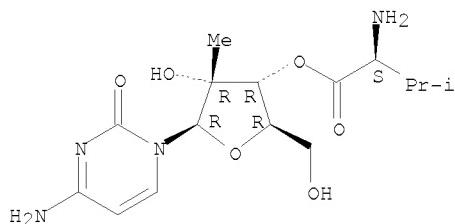
O=CH-OH

RN 642075-62-5 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, (2E)-2-butenedioate (salt)
(9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

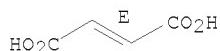
Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



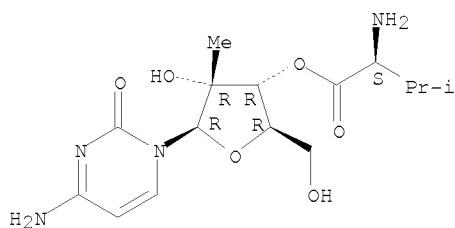
RN 642075-63-6 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, propanoate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

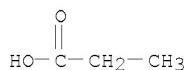
McIntosh

Absolute stereochemistry. Rotation (+).



CM 2

CRN 79-09-4
CMF C3 H6 O2

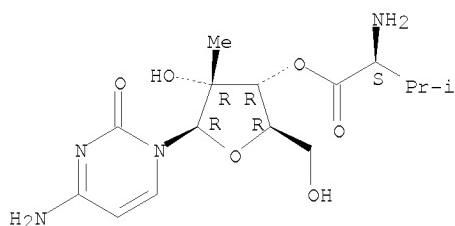


RN 642075-64-7 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydroxyacetate (salt) (9CI)
(CA INDEX NAME)

CM 1

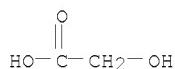
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 79-14-1
CMF C2 H4 O3

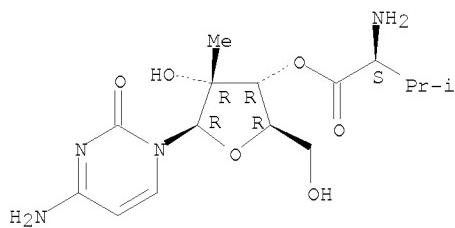


RN 642075-65-8 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-hydroxypropanoate (salt)
(9CI) (CA INDEX NAME)

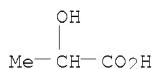
CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



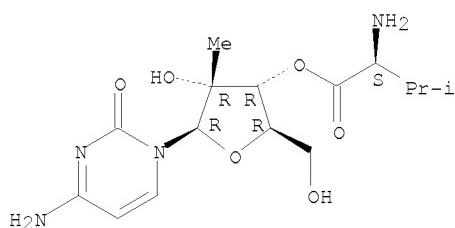
CM 2

CRN 50-21-5
CMF C₃ H₆ O₃RN 642075-66-9 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-oxopropanoate (salt) (9CI)
(CA INDEX NAME)

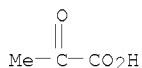
CM 1

CRN 640281-90-9
CMF C₁₅ H₂₄ N₄ O₆

Absolute stereochemistry. Rotation (+).



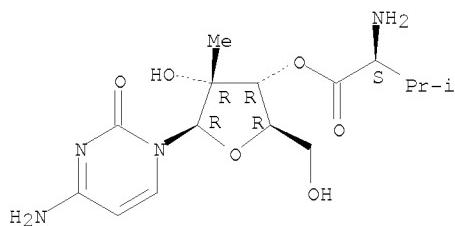
CM 2

CRN 127-17-3
CMF C₃ H₄ O₃RN 642075-67-0 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, ethanedioate (salt) (9CI)
(CA INDEX NAME)

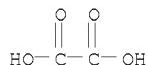
CM 1

CRN 640281-90-9
CMF C₁₅ H₂₄ N₄ O₆

Absolute stereochemistry. Rotation (+).



CM 2

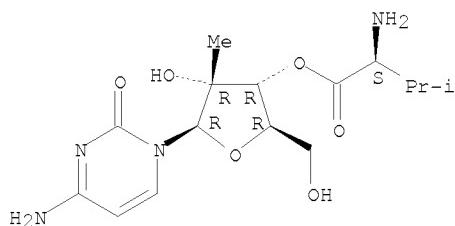
CRN 144-62-7
CMF C₂ H₂ O₄

RN 642075-68-1 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, (2*Z*)-2-butenedioate (salt)
 (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9
CMF C₁₅ H₂₄ N₄ O₆

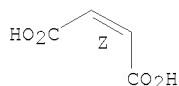
Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-16-7
CMF C₄ H₄ O₄

Double bond geometry as shown.

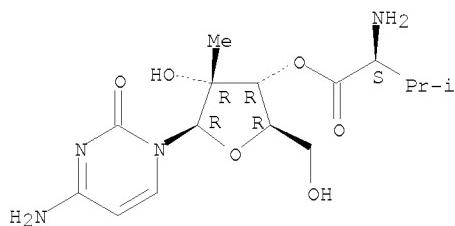


RN 642075-69-2 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-hydroxybenzoate (salt)
 (9CI) (CA INDEX NAME)

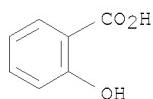
CM 1

CRN 640281-90-9
CMF C₁₅ H₂₄ N₄ O₆

Absolute stereochemistry. Rotation (+).



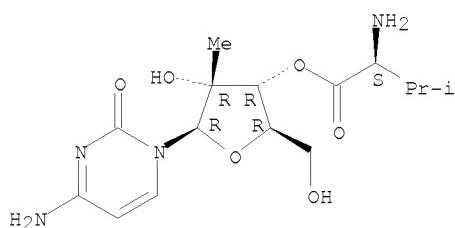
CM 2

CRN 69-72-7
CMF C7 H6 O3RN 642075-70-5 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, sulfate (salt) (9CI) (CA INDEX NAME)

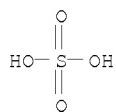
CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



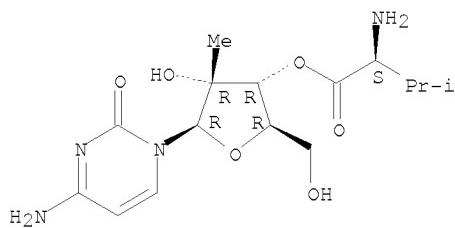
CM 2

CRN 7664-93-9
CMF H2 O4 SRN 642075-71-6 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, nitrate (salt) (9CI) (CA INDEX NAME)

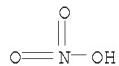
CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



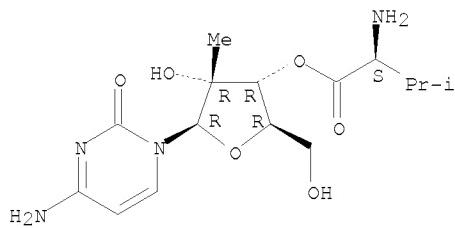
CM 2

CRN 7697-37-2
CMF H N O3RN 642075-72-7 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, carbonate (salt) (9CI) (CA INDEX NAME)

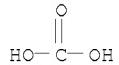
CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

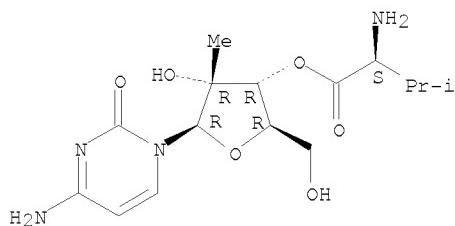
Absolute stereochemistry. Rotation (+).



CM 2

CRN 463-79-6
CMF C H2 O3RN 642075-74-9 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrobromide (9CI) (CA INDEX NAME)

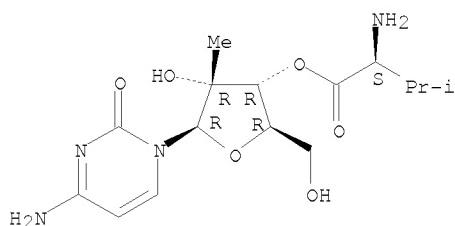
Absolute stereochemistry. Rotation (+).



● x HBr

RN 642075-75-0 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydriodide (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



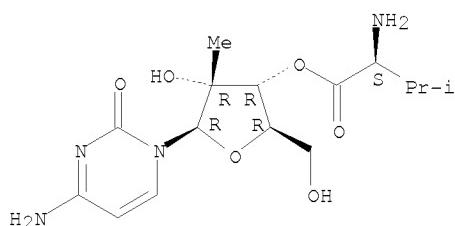
● x HI

RN 642075-76-1 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, carbonate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

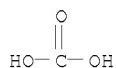
CRN 640281-90-9
 CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 463-79-6
 CMF C H2 O3



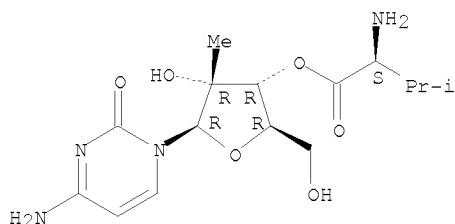
10/609,298

RN 642075-77-2 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, phosphate (salt) (9CI) (CA INDEX NAME)

CM 1

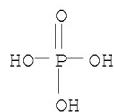
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 7664-38-2
CMF H3 O4 P

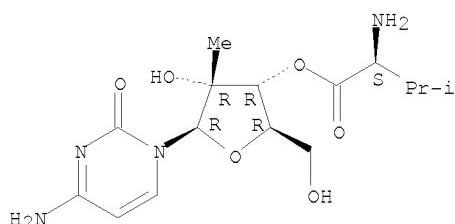


IT 640281-90-9P
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ribofuranosylcytidine methylvaline ester for treatment of flaviviridae infections)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

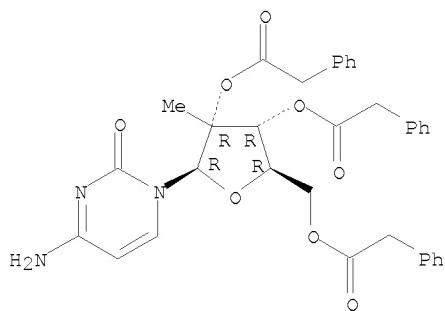


IT 642075-41-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(ribofuranosylcytidine methylvaline ester for treatment of flaviviridae infections)

RN 642075-41-0 CAPLUS

CN Cytidine, 2'-C-methyl-, 2',3',5'-tris(benzeneacetate) (9CI) (CA INDEX NAME)

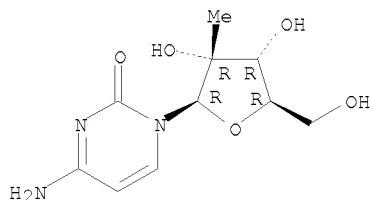
Absolute stereochemistry.



IT 20724-73-6P 640725-70-8P 642075-42-1P
 642075-43-2P 642075-44-3P 642075-48-7P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (ribofuranosylcytidine methylvaline ester for treatment of
 flaviviridae infections)

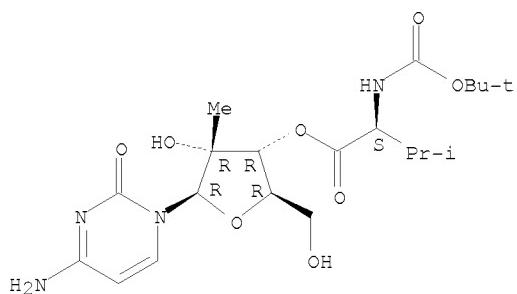
RN 20724-73-6 CAPLUS
 CN Cytidine, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



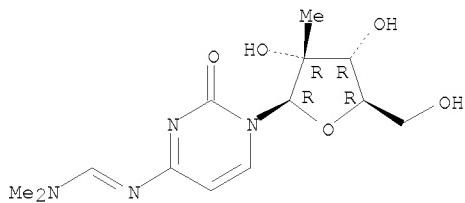
RN 640725-70-8 CAPLUS
 CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with
 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry.



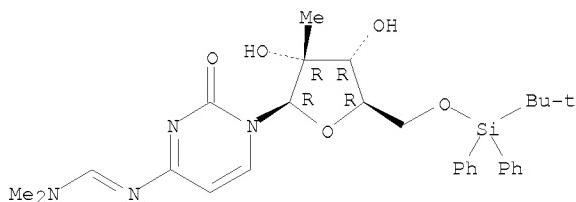
RN 642075-42-1 CAPLUS
 CN Cytidine, N-[(dimethylamino)methylene]-2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry unknown.



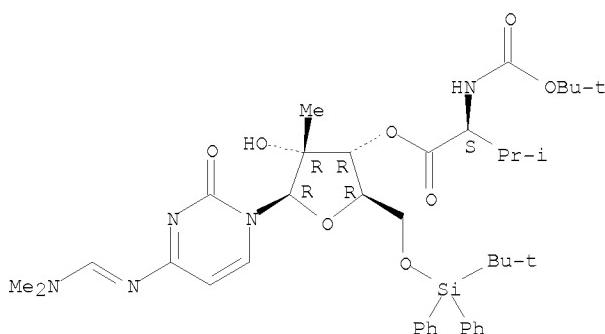
RN 642075-43-2 CAPLUS
 CN Cytidine, N-[(dimethylamino)methylene]-5'-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry unknown.



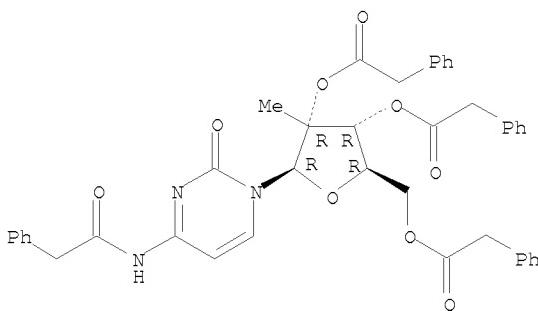
RN 642075-44-3 CAPLUS
 CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with 5'-O-[(1,1-dimethylethyl)diphenylsilyl]-N-[(dimethylamino)methylene]-2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry unknown.



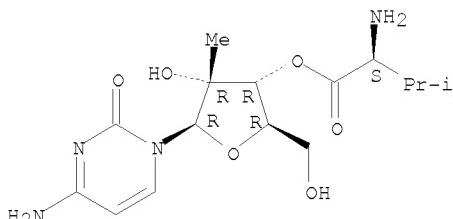
RN 642075-48-7 CAPLUS
 CN Cytidine, 2'-C-methyl-N-(phenylacetyl)-, 2',3',5'-tris(benzeneacetate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 640725-71-9P
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (ribofuranosylcytidine methylvaline ester for treatment of flaviviridae infections)
 RN 640725-71-9 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

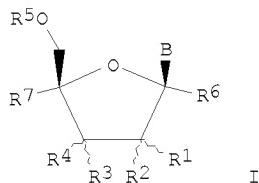


● 2 HCl

L6 ANSWER 53 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2004:2898 CAPLUS
 DN 140:42424
 TI Preparation of nucleoside derivatives as inhibitors of RNA-dependent RNA viral polymerase
 IN Carroll, Steven S.; Olsen, David B.; Durette, Philippe L.; Bhat, Balkrishen; Dande, Prasad; Eldrup, Anne B.
 PA Merck & Co., Inc., USA; Isis Pharmaceuticals, Inc.
 SO PCT Int. Appl., 43 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| PI WO 2004000858 | A2 | 20031231 | WO 2003-US19172 | 20030617 |
| WO 2004000858 | A3 | 20050512 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, IU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2488534 | A1 | 20031231 | CA 2003-2488534 | 20030617 |
| AU 2003269890 | A1 | 20040106 | AU 2003-269890 | 20030617 |

| | | | | |
|--|----|----------|----------------|----------|
| EP 1551421 | A2 | 20050713 | EP 2003-751777 | 20030617 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| JP 2005530843 | T | 20051013 | JP 2004-515870 | 20030617 |
| US 20070004669 | A1 | 20070104 | US 2006-517295 | 20060615 |
| PRAI US 2002-390579P | P | 20020621 | | |
| WO 2003-US19172 | W | 20030617 | | |
| OS MARPAT 140:42424 | | | | |
| GI | | | | |



AB The present invention provides nucleoside compds. I, wherein B is nucleobase; R1 is fluoromethyl, difluoromethyl, trifluoromethyl; R2 is H, F, amino, OH, SH, alkoxy, alkylcarbonyloxy, alkyl; R3 and R4 are independently H, Cn, N3, halogen, OH, SH, amino, alkoxy, alkylcarconyloxy, alkenyl, alkynyl; R5 is H, alkylcarbonyl, P3O9H4, P2O6H3, phosphophonyl; R6 and R7 independently H, Me, hydroxymethyl, fluoromethyl; and certain derivs. thereof which are inhibitors of RNA-dependent RNA viral polymerase. These compds. are inhibitors of RNA-dependent RNA viral replication and are useful for the treatment of RNA-dependent RNA viral infection. They are particularly useful as inhibitors of hepatitis C virus (HCV) NS5B polymerase, as inhibitors of HCV replication, and/or for the treatment of hepatitis C infection. The invention also describes pharmaceutical compns. containing such nucleoside compds. alone or in combination with other agents active against RNA-dependent RNA viral infection, in particular HCV infection. Also disclosed are methods of inhibiting RNA-dependent RNA polymerase, inhibiting RNA-dependent RNA replication, and/or treating RNA-dependent RNA viral infection with the nucleoside compds. of the present invention. Thus, 2-amino-9-(2-C-fluoromethyl-β-D-ribofuranosyl)-3,9-dihdropurin-6-one was prepared and tested as inhibitor of RNA-dependent RNA viral polymerase. Title compds. tested in the HCV NS5B polymerase assay exhibited IC50's less than 100 μmol.

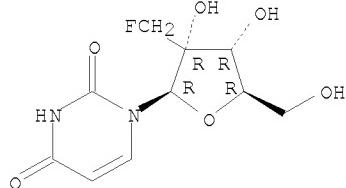
IT 510765-51-2P 636581-91-4P 636581-92-5P
636581-93-6P 636582-01-9P 636582-02-0P
636582-03-1P 636582-04-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nucleoside derivs. as inhibitors of RNA-dependent RNA viral polymerase)

RN 510765-51-2 CAPLUS

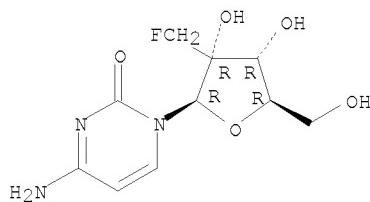
CN Uridine, 2'-C-(fluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.



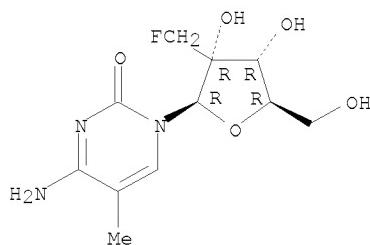
RN 636581-91-4 CAPLUS
CN Cytidine, 2'-C-(fluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



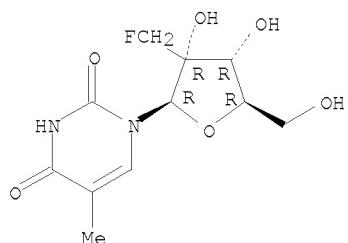
RN 636581-92-5 CAPLUS
CN Cytidine, 2'-C-(fluoromethyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



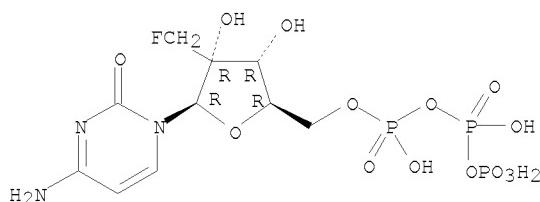
RN 636581-93-6 CAPLUS
CN Uridine, 2'-C-(fluoromethyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



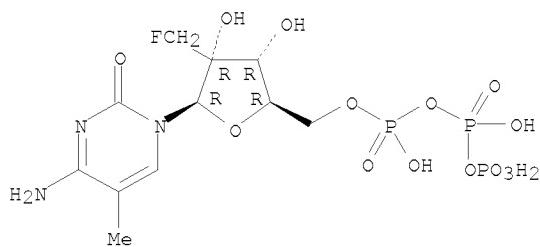
RN 636582-01-9 CAPLUS
CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-C-(fluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



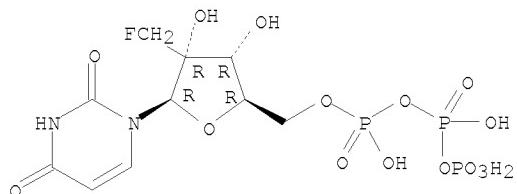
RN 636582-02-0 CAPLUS
CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-C-(fluoromethyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



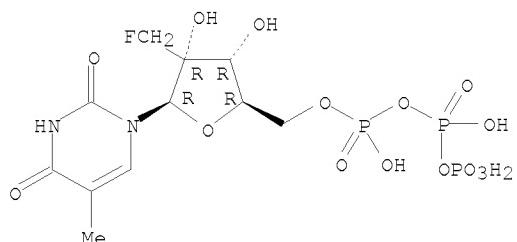
RN 636582-03-1 CAPLUS
 CN Uridine 5'-(tetrahydrogen triphosphate), 2'-C-(fluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 636582-04-2 CAPLUS
 CN Uridine 5'-(tetrahydrogen triphosphate), 2'-C-(fluoromethyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 54 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2003:892793 CAPLUS
 DN 139:365176
 TI Preparation of nucleoside derivatives for treating hepatitis C virus infection
 IN Roberts, Christopher Don; Dyatkina, Natalia B.; Keicher, Jesse D.; Liehr, Sebastian Johannes Reinhard; Hanson, Eric Jason
 PA Genelabs Technologies, Inc., USA
 SO PCT Int. Appl., 182 pp.
 CODEN: PIXXD2

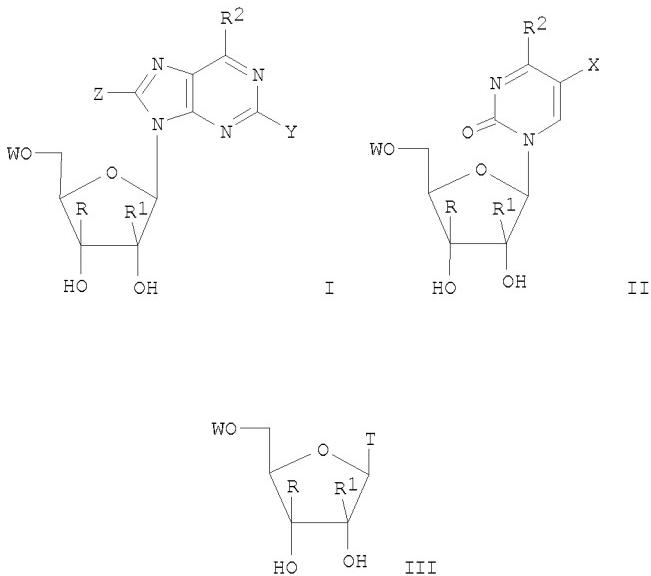
DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|----------|
| PI | WO 2003093290 | A2 | 20031113 | WO 2003-US14237 | 20030506 |
| | WO 2003093290 | A3 | 20040318 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 CA 2484921 A1 20031113 CA 2003-2484921 20030506
 AU 2003232071 A1 20031117 AU 2003-232071 20030506
 US 20040063658 A1 20040401 US 2003-431631 20030506
 EP 1501850 A2 20050202 EP 2003-747674 20030506
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
 BR 2003009581 A 20050329 BR 2003-9581 20030506
 CN 1653077 A 20050810 CN 2003-810239 20030506
 JP 2005530759 T 20051013 JP 2004-501429 20030506
 NZ 536123 A 20060929 NZ 2003-536123 20030506
 MX 2004PA10983 A 20050214 MX 2004-PA10983 20041105
 NO 2004005247 A 20041130 NO 2004-5247 20041130
 PRAI US 2002-378624P P 20020506
 US 2002-392871P P 20020628
 WO 2003-US14237 W 20030506
 OS MARPAT 139:365176
 GI



AB Nucleosides I-III, wherein R and R1 are independently H, alkyl, alkenyl, alkynyl, provided that R and R1 are not both H; R2 is alkyl, cycloalkyl, alkenyl, alkynyl, acylamino, guanidino, amidino, thioacylamino, OH, alkoxy, halo, nitro, aryl, heteroaryl, substituted amine; W is H, phosphate, phosphonate, acyl, alkyl, sulfonate, lipid, amino acid, sugar residue, peptide, cholesterol; X is H, halo, alkyl, substituted amine; Y is H, halo, OH, alkylthio, substituted amine; Z is H, halo, OH, alkyl, substituted amine; T is nucleobase, were prepared as HCV RNA polymerase inhibitors and for treating hepatitis C virus infections. Thus, 2-(4-amino-pyrrolo[3,2-c]pyridin-1-yl)-5-hydroxymethyl-3-methyltetrahydro-furan-3,4-diol was prepared for treating hepatitis C virus infections (no data). Different kind of formulation such as tablet, capsule, suspension, injectable, and suppository formulation are reported.

IT 31448-54-1P 119410-84-3P 622380-51-2P
 622380-52-3P 622380-56-7P 622380-57-8P
 622380-59-0P 622380-60-3P 622380-61-4P
 622380-89-6P 622380-90-9P 622381-09-3P
 622381-10-6P

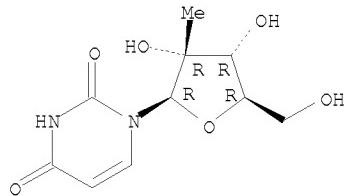
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nucleoside derivs. for treating hepatitis C virus infection)

RN 31448-54-1 CAPLUS

CN Uridine, 2'-C-methyl- (CA INDEX NAME)

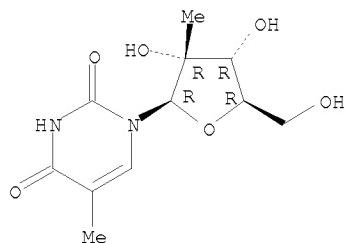
Absolute stereochemistry. Rotation (+).



RN 119410-84-3 CAPLUS

CN Uridine, 5-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

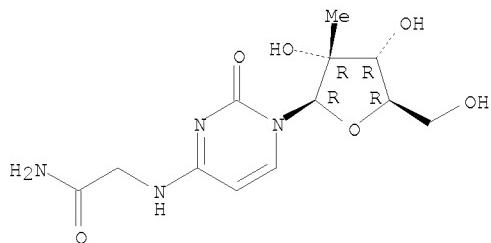
Absolute stereochemistry. Rotation (+).



RN 622380-51-2 CAPLUS

CN Cytidine, N-(2-amino-2-oxoethyl)-2'-C-methyl- (9CI) (CA INDEX NAME)

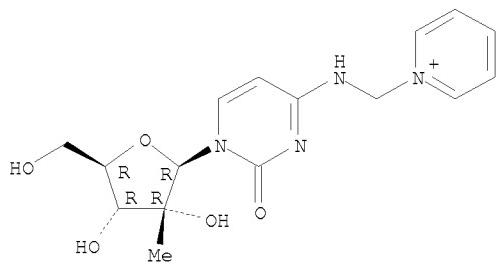
Absolute stereochemistry.



RN 622380-52-3 CAPLUS

CN Pyridinium, 1-[[[1,2-dihydro-1-(2-C-methyl-β-D-ribofuranosyl)-2-oxo-4-pyrimidinyl]amino]methyl]- (CA INDEX NAME)

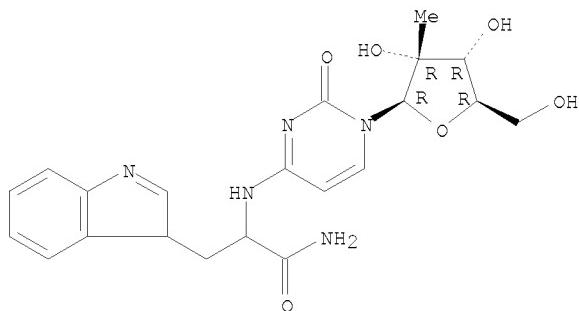
Absolute stereochemistry.



10/609, 298

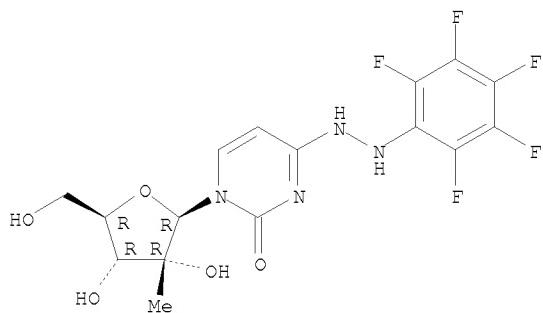
RN 622380-56-7 CAPLUS
CN Cytidine, N-[2-amino-1-(3H-indol-3-ylmethyl)-2-oxoethyl]-2'-C-methyl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



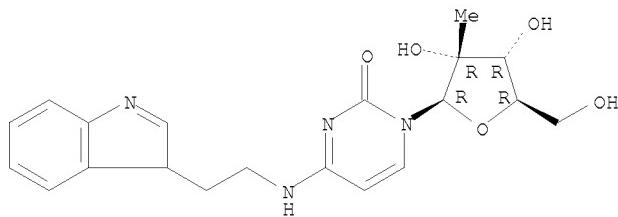
RN 622380-57-8 CAPLUS
CN Uridine, 2'-C-methyl-, 4-[(pentafluorophenyl)hydrazone] (9CI) (CA INDEX
NAME)

Absolute stereochemistry.



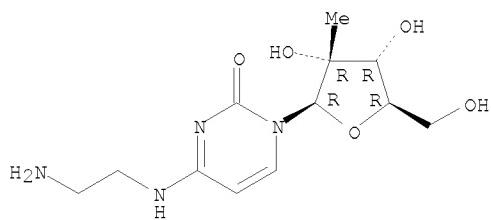
RN 622380-59-0 CAPLUS
CN Cytidine, N-[2-(3H-indol-3-yl)ethyl]-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



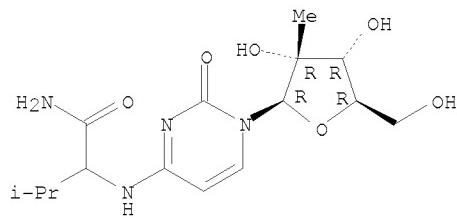
RN 622380-60-3 CAPLUS
CN Cytidine, N-(2-aminoethyl)-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



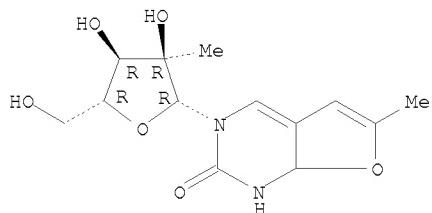
RN 622380-61-4 CAPLUS
CN Cytidine, N-[1-(aminocarbonyl)-2-methylpropyl]-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



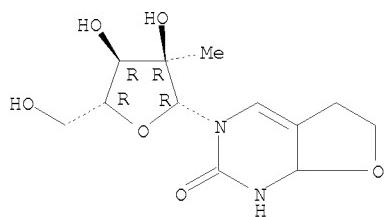
RN 622380-89-6 CAPLUS
CN Furo[2,3-d]pyrimidin-2(1H)-one, 3,7a-dihydro-6-methyl-3-(2-C-methyl-beta-D-ribofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry.



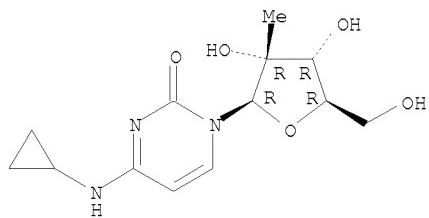
RN 622380-90-9 CAPLUS
CN Furo[2,3-d]pyrimidin-2(1H)-one, 3,5,6,7a-tetrahydro-3-(2-C-methyl-beta-D-ribofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry.



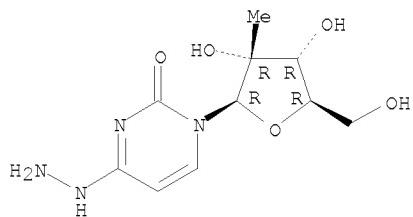
RN 622381-09-3 CAPLUS
CN Cytidine, N-cyclopropyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



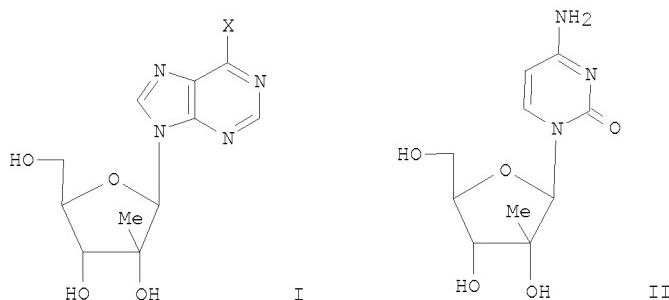
RN 622381-10-6 CAPLUS
 CN Uridine, 2'-C-methyl-, 4-hydrazone (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 55 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2003:591195 CAPLUS
 DN 139:133789
 TI Preparation of sugar modified nucleosides as antiviral agents
 IN Hong, Zhi; An, Haoyun; Ding, Yili; Girardet, Jean-luc; Zhong, Weidong
 PA Ribapharm Inc., USA
 SO PCT Int. Appl., 33 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 4

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|------------------|----------|
| PI | WO 2003062255 | A2 | 20030731 | WO 2002-US231556 | 20021002 |
| | WO 2003062255 | A3 | 20060908 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1572705 | A2 | 20050914 | EP 2002-776103 | 20021002 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| | US 20070032448 | A1 | 20070208 | US 2006-535742 | 20060925 |
| PRAI | US 2002-350296P | P | 20020117 | | |
| | US 2002-391800P | P | 20020626 | | |
| | WO 2002-US31556 | W | 20021002 | | |
| OS | MARPAT 139:133789 | | | | |
| GI | | | | | |



AB Various 2'-modified nucleoside analogs I and II wherein X is NH₂, NHMe, NMe₂, OMe, SMe, and corresponding prodrugs are provided, and particularly contemplated methods of use include use as antiviral agents, and especially as antiviral agents against HCV.

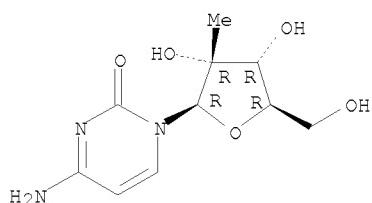
IT 20724-73-6 31448-54-1 119410-84-3
565451-07-2 565451-08-3 565451-09-4
565451-10-7 565451-11-8

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of sugar modified nucleosides as antiviral agents)

RN 20724-73-6 CAPLUS

CN Cytidine, 2'-C-methyl- (CA INDEX NAME)

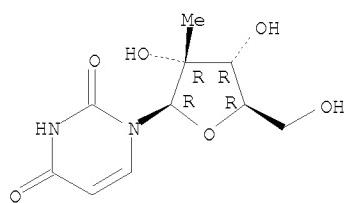
Absolute stereochemistry.



RN 31448-54-1 CAPLUS

CN Uridine, 2'-C-methyl- (CA INDEX NAME)

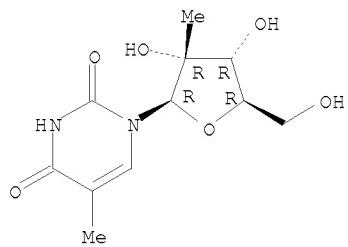
Absolute stereochemistry. Rotation (+).



RN 119410-84-3 CAPLUS

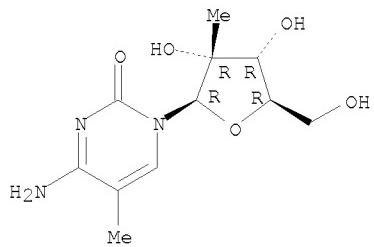
CN Uridine, 5-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



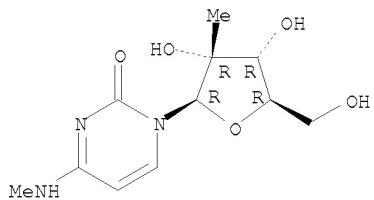
RN 565451-07-2 CAPLUS
CN Cytidine, 5-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



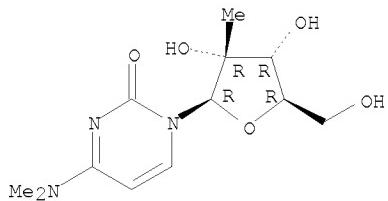
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CN Cytidine, N-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



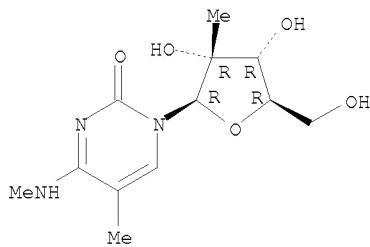
RN 565451-09-4 CAPLUS
CN Cytidine, N,N-dimethyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



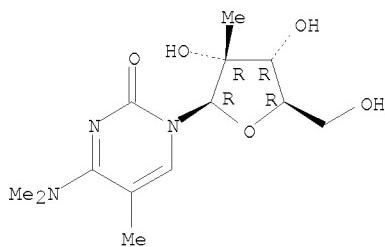
RN 565451-10-7 CAPLUS
CN Cytidine, N,5-dimethyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 565451-11-8 CAPLUS
 CN Cytidine, N,N,5-trimethyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

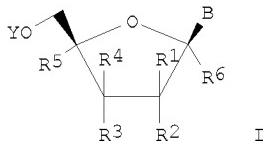


L6 ANSWER 56 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2002:555629 CAPLUS
 DN 137:125359
 TI Preparation of nucleoside derivatives as inhibitors of RNA-dependent RNA viral polymerase
 IN Carroll, Steven S.; Lafemina, Robert L.; Hall, Dawn L.; Himmelberger, Amy L.; Kuo, Lawrence C.; MacCoss, Malcolm; Olsen, David B.; Rutkowski, Carrie A.; Tomassini, Joanne E.; An, Haoyun; Bhat, Balkrishen; Bhat, Neelima; Cook, Phillip Dan; Eldrup, Anne B.; Guinossio, Charles J.; Prhavc, Marija; Prakash, Thazha P.
 PA Merck & Co., Inc., USA; Isis Pharmaceuticals, Inc.
 SO PCT Int. Appl., 235 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|----------|
| PI | WO 2002057425 | A2 | 20020725 | WO 2002-US1531 | 20020118 |
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| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2433878 | A1 | 20020725 | CA 2002-2433878 | 20020118 |
| | AU 2002243600 | A1 | 20020730 | AU 2002-243600 | 20020118 |
| | AU 2002243600 | B2 | 20060928 | | |
| | US 20020147160 | A1 | 20021010 | US 2002-52318 | 20020118 |
| | US 6777395 | B2 | 20040817 | | |
| | CN 1498221 | A | 20040519 | CN 2002-806977 | 20020118 |
| | JP 2004532184 | T | 20041021 | JP 2002-558479 | 20020118 |
| | EP 1539188 | A2 | 20050615 | EP 2002-709095 | 20020118 |
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| ES 2278009 | T3 | 20070801 | ES 2002-709299 | 20020118 |
| TW 261056 | B | 20060901 | TW 2002-91100893 | 20020121 |
| US 20040072788 | A1 | 20040415 | US 2003-431657 | 20030507 |
| ZA 2003005078 | A | 20040521 | ZA 2003-5078 | 20030630 |
| US 20040067901 | A1 | 20040408 | US 2003-688691 | 20031017 |
| US 7125855 | B2 | 20061024 | | |
| US 20040110717 | A1 | 20040610 | US 2004-250873 | 20040116 |
| US 7105499 | B2 | 20060912 | | |
| US 20050272676 | A1 | 20051208 | US 2005-200499 | 20050809 |
| US 20060205686 | A1 | 20060914 | US 2005-236224 | 20050927 |
| US 20060264390 | A1 | 20061123 | US 2006-496338 | 20060731 |
| US 7202224 | B2 | 20070410 | | |
| US 20070275912 | A1 | 20071129 | US 2006-643464 | 20061221 |
| JP 2007224045 | A | 20070906 | JP 2007-115345 | 20070425 |
| PRAI US 2001-263313P | P | 20010122 | | |
| US 2001-282069P | P | 20010406 | | |
| US 2001-299320P | P | 20010619 | | |
| US 2001-344528P | P | 20011025 | | |
| EP 2002-709299 | A3 | 20020118 | | |
| JP 2002-558479 | A3 | 20020118 | | |
| US 2002-52318 | A3 | 20020118 | | |
| WO 2002-US1531 | W | 20020118 | | |
| US 2003-431657 | B1 | 20030507 | | |
| US 2003-688691 | A1 | 20031017 | | |
| US 2005-200499 | B1 | 20050809 | | |

OS MARPAT 137:125359
GI

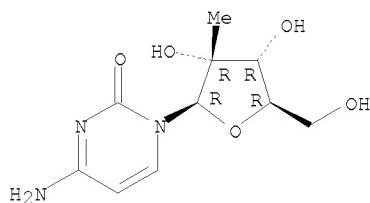


AB The present invention provides the preparation of nucleoside compds. I, wherein B is nucleobase, Y is H, alkylcarbonyl, phosphate; R1 is H, alkenyl, alkynyl, alkyl; R2 and R3 are independently H, OH, halogen, alkyl, alkoxy, alkenyloxy, alkylthio, alkylcarbonyloxy, aryloxycarbonyl, azido, amino, alkylamino; R1 and R2 together with the carbon atom to which they are attached form a 3- to 6-membered heterocycle; R4 is H, OH, SH, NH₂, alkylamino, cycloalkylamino, halogen, alkyl, alkoxy, CF₃; R5 and R6 are independently H, hydroxymethyl, Me, fluoromethyl; and certain derivs. thereof which are inhibitors of RNA-dependent RNA viral polymerase. These compds. are inhibitors of RNA-dependent RNA viral replication and are useful for the treatment of RNA-dependent RNA viral infection. They are particularly useful as inhibitors of hepatitis C virus (HCV) NS5B polymerase, as inhibitors of HCV replication, and/or for the treatment of hepatitis C infection. The invention also describes pharmaceutical compns. containing such nucleoside compds. alone or in combination with other agents active against RNA-dependent RNA viral infection, in particular HCV infection. Also disclosed are methods of inhibiting RNA-dependent RNA polymerase, inhibiting RNA-dependent RNA viral replication, and/or treating RNA-dependent RNA viral infection with the nucleoside compds. of the present invention. Thus, 4-amino-1-(2-C-methyl-β-D-ribofuranosyl)-1H-pyrazolo[3,4-d]pyrimidine was prepared as inhibitors of RNA-dependent RNA viral polymerase. Representative compds. tested in the HCV NS5B polymerase assay exhibited IC₅₀'s less than 100 μM. The compds. of the present invention were also evaluated for their ability to affect the replication of Hepatitis C Virus RNA in cultured hepatoma (HuH-7) cells containing a sub-genomic HCV Replicon.

IT 20724-73-6P 114262-49-6P 374750-28-4P
444019-82-3P 444020-83-1P 444022-03-1P
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nucleoside derivs. as inhibitors of RNA-dependent human RNA

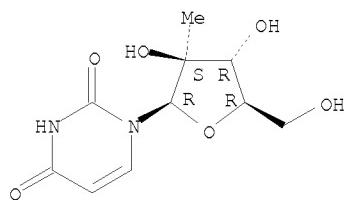
viral polymerase)
RN 20724-73-6 CAPLUS
CN Cytidine, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



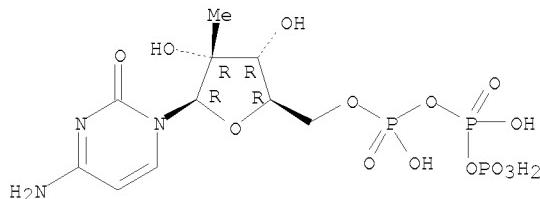
RN 114262-49-6 CAPLUS
CN 2, 4(1H, 3H)-Pyrimidinedione, 1-(2-C-methyl-β-D-arabinofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



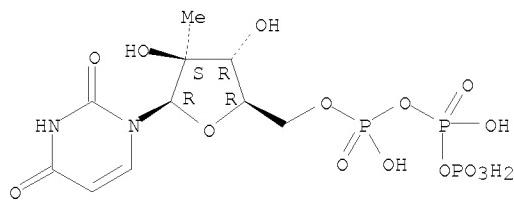
RN 374750-28-4 CAPLUS
CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



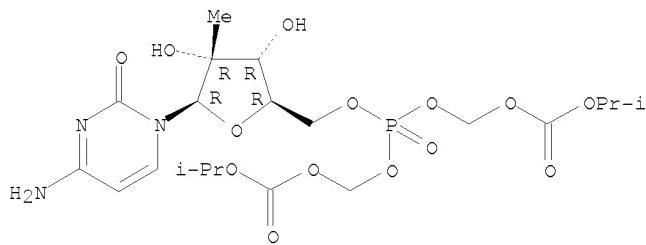
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CN 2, 4(1H, 3H)-Pyrimidinedione, 1-[5-O-[hydroxy[[hydroxy(phosphonoxy)phosphinyl]oxy]phosphinyl]-2-C-methyl-β-D-arabinofuranosyl]- (CA INDEX NAME)

Absolute stereochemistry.



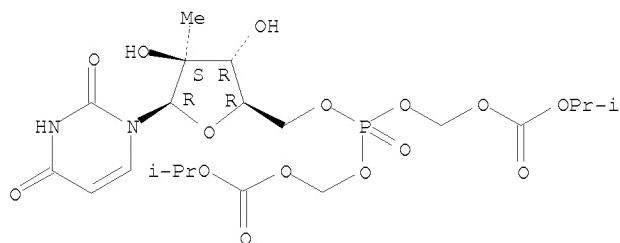
RN 444020-83-1 CAPLUS
CN 5'-Cytidylic acid, 2'-C-methyl-, bis[[[(1-methylethoxy)carbonyl]oxy]methyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 444022-03-1 CAPLUS
 CN 2,4(1H,3H)-Pyrimidinedione, 1-[2-C-methyl-5-O-[7-methyl-1-[(1-methylethoxy)carbonyl]oxy]methoxy]-1-oxido-5-oxo-2,4,6-trioxa-1-phosphaoct-1-yl]-β-D-arabinofuranosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



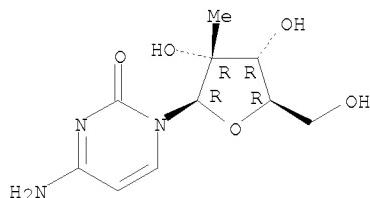
L6 ANSWER 57 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2001:886155 CAPLUS
 DN 136:590
 TI Methods and compositions using modified nucleosides for treating
 flaviviruses and pestiviruses
 IN Sommadossi, Jean-Pierre; Lacolla, Paolo
 PA Novirio Pharmaceuticals Limited, Cayman I.; Universita Degli Studi Di
 Cagliari
 SO PCT Int. Appl., 302 pp.
 CODEN: PIXXD2

DT Patent
 LA English
 FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|--|------|----------|-----------------|----------|
| PI | WO 2001092282 | A2 | 20011206 | WO 2001-US16687 | 20010523 |
| | WO 2001092282 | A3 | 20020502 | | |
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LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
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UZ, VN, YU, ZA, ZW
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CA 2410579 | | | | |
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| | EP 1294735 | A2 | 20030326 | EP 2001-952131 | 20010523 |
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| US | 6812219 | B2 | 20041102 | | |
| CN | 1468249 | A | 20040114 | CN 2001-813182 | 20010523 |
| BR | 2001011196 | A | 20040406 | BR 2001-11196 | 20010523 |
| JP | 2004510698 | T | 20040408 | JP 2002-500895 | 20010523 |
| NZ | 536570 | A | 20060831 | NZ 2001-536570 | 20010523 |
| EP | 1736478 | A1 | 20061227 | EP 2006-75198 | 20010523 |
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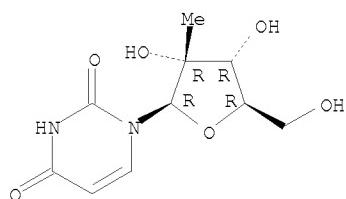
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| AP 1727 | A | 20070430 | AP 2002-2705 | 20010523 |
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| NZ 547204 | A | 20080131 | NZ 2001-547204 | 20010523 |
| NO 2002005600 | A | 20030117 | NO 2002-5600 | 20021121 |
| MX 2002PA11691 | A | 20040517 | MX 2002-PA11691 | 20021126 |
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| ZA 2002010112 | A | 20040623 | ZA 2002-10112 | 20021212 |
| US 20040063622 | A1 | 20040401 | US 2003-602693 | 20030620 |
| US 7148206 | B2 | 20061212 | | |
| US 20040097462 | A1 | 20040520 | US 2003-602692 | 20030620 |
| US 7101861 | B2 | 20060905 | | |
| US 20040102414 | A1 | 20040527 | US 2003-602694 | 20030620 |
| US 7105493 | B2 | 20060912 | | |
| US 20060166865 | A1 | 20060727 | US 2003-602135 | 20030620 |
| US 7163929 | B2 | 20070116 | | |
| US 20070037773 | A1 | 20070215 | US 2006-527124 | 20060925 |
| AU 2007202602 | A1 | 20070719 | AU 2007-202602 | 20070607 |
| KR 2008021797 | A | 20080307 | KR 2008-701618 | 20080121 |
| PRAI US 2000-207674P | P | 20000526 | | |
| US 2001-283276P | P | 20010411 | | |
| CN 2001-813182 | A3 | 20010523 | | |
| EP 2001-952131 | A3 | 20010523 | | |
| US 2001-863816 | A3 | 20010523 | | |
| WO 2001-US16687 | W | 20010523 | | |
| KR 2002-715794 | A3 | 20021122 | | |
| US 2003-602135 | A1 | 20030620 | | |
| OS MARPAT 136:590 | | | | |
| AB | A method and composition are provided for treating a host infected with flavivirus or pestivirus, comprising administering an effective amount of a 1', 2' or 3'-modified nucleoside or a pharmaceutically acceptable salt or prodrug thereof. | | | |
| IT | 20724-73-6 31448-54-1 119410-84-3
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleoside derivs. for treating flaviviruses and pestiviruses) | | | |
| RN | 20724-73-6 CAPLUS | | | |
| CN | Cytidine, 2'-C-methyl- (CA INDEX NAME) | | | |

Absolute stereochemistry.



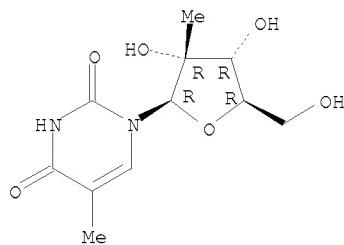
RN 31448-54-1 CAPLUS
CN Uridine, 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



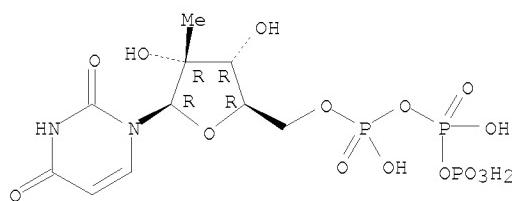
RN 119410-84-3 CAPLUS
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Absolute stereochemistry. Rotation (+).



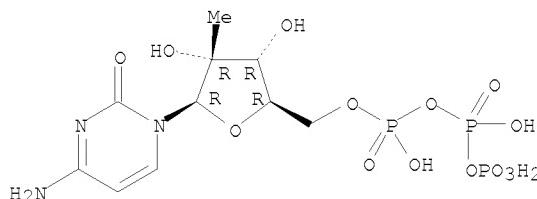
IT 125911-76-4 374750-28-4
 RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); BIOL (Biological study)
 (nucleoside derivs. for treating flaviviruses and pestiviruses)
 RN 125911-76-4 CAPLUS
 CN Uridine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 374750-28-4 CAPLUS
 CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (CA INDEX NAME)

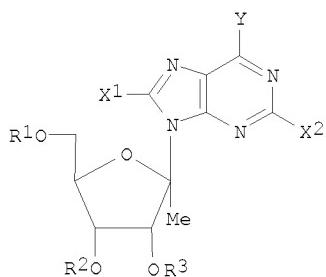
Absolute stereochemistry.



L6 ANSWER 58 OF 58 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2001:868467 CAPLUS
 DN 136:6296
 TI Preparation of antiviral nucleosides and methods for treating hepatitis C virus
 IN Sommadossi, Jean-Pierre; Lacolla, Paulo
 PA Novirio Pharmaceuticals Limited, Cayman I.; Universita degli Studi di Cagliari
 SO PCT Int. Appl., 296 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
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| PI WO 2001090121 | A2 | 20011129 | WO 2001-US16671 | 20010523 |
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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, | | | | |

RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
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 CA 2409613 A1 20011129 CA 2001-2409613 20010523
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 US 20030050229 A1 20030313 US 2001-864078 20010523
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 JP 2004533401 T 20041104 JP 2001-586308 20010523
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 US 20040097461 A1 20040520 US 2003-602691 20030620
 US 20040101535 A1 20040527 US 2003-602976 20030620
 US 7169766 B2 20070130
 US 20050124532 A1 20050609 US 2003-602142 20030620
 US 20050137161 A1 20050623 US 2003-602136 20030620
 US 7157441 B2 20070102
 AU 2006203121 A1 20060810 AU 2006-203121 20060721
 AU 2006203122 A1 20060810 AU 2006-203122 20060721
 KR 2007036806 A 20070403 KR 2007-706401 20070320
 NO 2007003151 A 20030106 NO 2007-3151 20070620
 IN 2007DN09886 A 20080125 IN 2007-DN9886 20071219
 IN 2007DN09890 A 20080125 IN 2007-DN9890 20071219
 IN 2007DN09896 A 20080208 IN 2007-DN9896 20071219
 KR 2008030670 A 20080404 KR 2008-703747 20080215
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 AU 2001-74906 A3 20010523
 EP 2001-941564 A3 20010523
 NZ 2001-522863 A3 20010523
 US 2001-864078 A1 20010523
 WO 2001-US16671 W 20010523
 KR 2002-715790 A3 20021122
 NO 2002-5627 A 20021122
 IN 2002-DN1184 A3 20021202
 OS MARPAT 136:6296
 GI



AB A method and composition for treating a host infected with hepatitis C comprising administering an effective hepatitis C treatment amount of a described 1'-, 2'- or 3'-modified

nucleosides I, wherein : R1-R3 and R are independently H, phosphate (including mono, di- or triphosphate and a stabilized phosphate prodrug); acyl; alkyl; sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the Ph group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered in vivo is capable of providing a compound wherein R1-R3 are independently H or phosphate; Y is hydrogen, bromo, chloro, fluoro, iodo, OR4, NR4R5 or SR4; X1 and X2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR4, NR4R5 or SR4; and R4 and R5 are independently hydrogen, acyl, alkyl or a pharmaceutically acceptable salt or prodrug thereof, is provided. Thus, I (R1-R3 = X1 = X2 = H, Y = NH₂) was prepared and tested in Cynomolgus monkeys as antiviral agent. Oral bioavailability in monkeys, bone human bone marrow toxicity (IC₅₀ > 10 μM), and mitochondrial toxicity, were reported .

IT 20724-73-6P 31448-54-1P 119410-84-3P

125911-76-4P 374750-28-4P

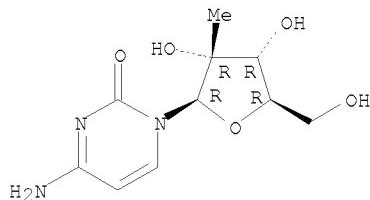
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of antiviral nucleosides and methods for treating hepatitis C virus)

RN 20724-73-6 CAPLUS

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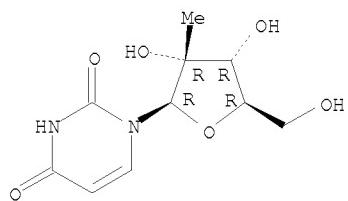
Absolute stereochemistry.



RN 31448-54-1 CAPLUS

CN Uridine, 2'-C-methyl- (CA INDEX NAME)

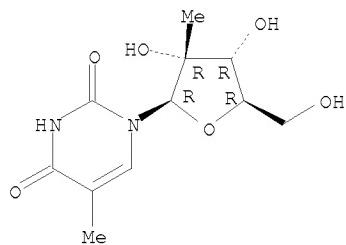
Absolute stereochemistry. Rotation (+).



RN 119410-84-3 CAPLUS

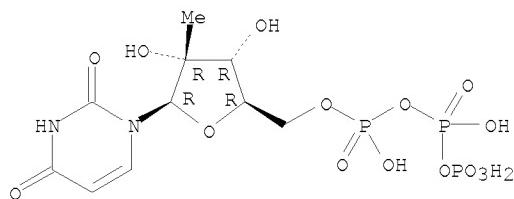
CN Uridine, 5-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



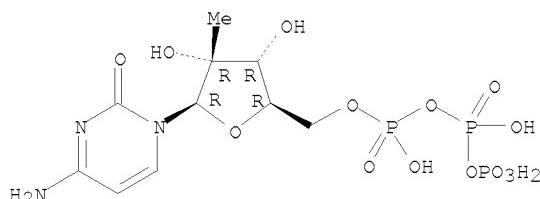
RN 125911-76-4 CAPLUS
 CN Uridine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 374750-28-4 CAPLUS
 CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



| | | | |
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| => file reg | | | |
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL | |
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 DICTIONARY FILE UPDATES: 6 JUN 2008 HIGHEST RN 1026208-38-7

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<http://www.cas.org/support/stngen/stndoc/properties.html>

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L7 STRUCTURE uploaded

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Structure attributes must be viewed using STN Express query preparation.

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SEARCH TIME: 00.00.01

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BATCH **COMPLETE**
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McIntosh

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<http://www.cas.org/legal/infopolicy.html>

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L10      74 L9

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        (FLAVIVIRUS OR FLAVIVIRUSES)
    501 PESTIVIRUS
    266 PESTIVIRUSES
    597 PESTIVIRUS
        (PESTIVIRUS OR PESTIVIRUSES)
    645 FLAVIVIRIDAE
14183 HCV
    24 HCVS
14187 HCV
        (HCV OR HCVS)
67218 HEPATITIS
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67218 HEPATITIS
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3835463 C
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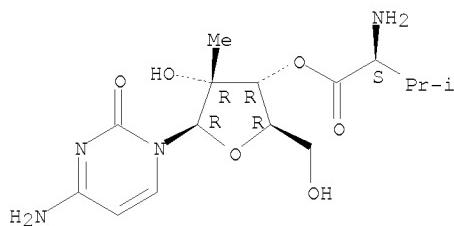
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L11 ANSWER 1 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2008:562068 CAPLUS
DN 148:509492
TI The hepatitis C virus replicon presents a higher barrier to resistance to nucleoside analogs than to nonnucleoside polymerase or protease inhibitors
AU McCown, Matthew F.; Rajyaguru, Sonal; Le Pogam, Sophie; Ali, Samir; Jiang, Wen-Rong; Kang, Hyunsoon; Symons, Julian; Cammack, Nick; Najera, Isabel
CS Department of HCV Biology, Virology Disease Biology Area, Roche Palo Alto LLC, Palo Alto, CA, 94304, USA
SO Antimicrobial Agents and Chemotherapy (2008), 52(5), 1604-1612
CODEN: AMACQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB Specific inhibitors of hepatitis C virus (HCV) replication that target the NS3/4A protease (e.g., VX-950) or the NS5B polymerase (e.g., R1479/R1626, PSI-6130/R7128, NM107/NM283, and HCV-796) have advanced into clin. development. Treatment of patients with VX-950 or HCV-796 rapidly selected for drug-resistant variants after a 14-day monotherapy treatment period. However, no viral resistance was identified after monotherapy with R1626 (prodrug of R1479) or NM283 (prodrug of NM107) after 14 days of monotherapy. Based upon the rapid selection of resistance to the protease and nonnucleoside inhibitors during clin. trials and the lack of selection of resistance to the nucleoside inhibitors, we used the replicon system to determine whether nucleoside inhibitors demonstrate a higher genetic barrier to resistance than protease and nonnucleoside inhibitors. Treatment of replicon cells with nucleoside inhibitors at 10 and 15 times the 50% effective concentration resulted in clearance of the replicon, while treatment with a nonnucleoside or protease inhibitor selected resistant colonies. In combination, the presence of a nucleoside inhibitor reduced the frequency of colonies resistant to the other classes of inhibitors. These results indicate that the HCV replicon presents a higher barrier to the selection of resistance to nucleoside inhibitors than to nonnucleoside or protease inhibitors. Furthermore, the combination of a nonnucleoside or protease inhibitor with a nucleoside polymerase inhibitor

could have a clear clin. benefit through the delay of resistance emergence.

- IT 640725-71-9, NM283
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (hepatitis C virus replicon presents a higher barrier to resistance to nucleoside analogs than to nonnucleoside polymerase or protease inhibitors)
- RN 640725-71-9 CAPLUS
- CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



●2 HCl

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

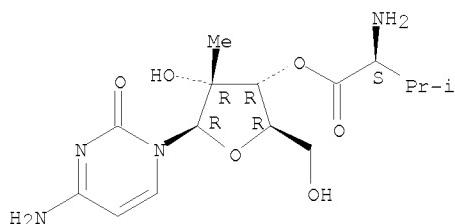
- L11 ANSWER 2 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2008:416659 CAPLUS
 DN 148:417879
 TI Compositions of immunostimulatory oligonucleotides as Toll-like receptor ligands and antiviral agents for therapeutic administration
 IN Vollmer, Jorg; Jurk, Marion; Uhlmann, Eugen; Debelak, Harald; Bratzler, Robert L.; Vicari, Alain
 PA Coley Pharmaceutical Group, Inc., USA; Coley Pharmaceutical G.m.b.H.; Coley Pharmaceutical Group, Ltd.
 SO PCT Int. Appl., 89pp.
 CODEN: PIXXD2
 DT Patent
 LA English

| FAN.CNT 1 | | | | |
|-----------|---|------|----------|--------------------------|
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| PI | WO 2008039538 | A2 | 20080403 | WO 2007-US21030 20070927 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
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- PRAI US 2006-847408P P 20060927
 AB The invention relates to methods and products for the treatment of viral infection using a combination of antiviral agents and Toll-like receptor (TLR) ligands. The TLR ligands comprise immunostimulatory oligonucleotides, preferably containing modifications selected from 8-oxo-rG, 8-bromo-dG, 8-bromo-dA, and isatoribine (Immunosine) with a 5'-5' linkage. The 8-modified guanine residues enhance immunostimulatory activity, particularly when present at the 5' end of the oligonucleotide. Combination of Ribavirin with an immunostimulatory CpG-containing oligonucleotide results in a decrease of interleukin-10 relative to interferon- α inducing activity. Further, Ribavirin and CpG

oligonucleotide improve survival in a mouse cancer model.
 IT 640281-90-9, Valopicitabine
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (compns. of immunostimulatory oligonucleotides as Toll-like receptor
 ligands and antiviral agents for therapeutic administration)
 RN 640281-90-9 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

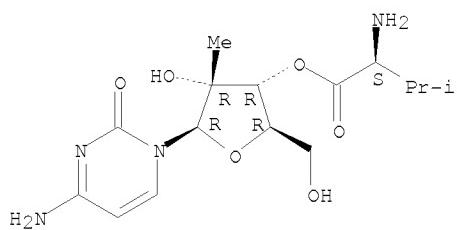
Absolute stereochemistry. Rotation (+).



L11 ANSWER 3 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2008:352859 CAPLUS
 DN 148:394354
 TI Compositions and methods for treatment of viral diseases
 IN Johansen, Lisa M.; Owens, Christopher M.; Mawhinney, Christina; Chappell,
 Todd W.; Brown, Alexander T.; Frank, Michael G.; Altmeyer, Ralf
 PA Combinatoria (Singapore) Pre. Ltd., Singapore
 SO PCT Int. Appl., 237pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

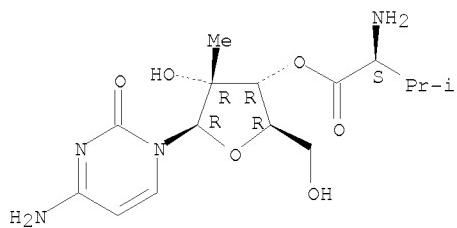
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| PI WO 2008033466 | A2 | 20080320 | WO 2007-US19932 | 20070913 |
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MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL,
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BY, KG, KZ, MD, RU, TJ, TM | | | | |
| PRAI US 2006-844463P | P | 20060914 | | |
| US 2006-874061P | P | 20061211 | | |
| AB | Based on the results of the authors screen identifying compds. and combinations of compds. having antiviral activity, the present invention features compns., methods, and kits useful in the treatment of viral diseases. In certain embodiments, the viral disease is caused by a single stranded RNA virus, a flaviviridae virus, or a hepatic virus. In particular embodiments, the viral disease is viral hepatitis (e.g., hepatitis A, hepatitis B, hepatitis C, hepatitis D, hepatitis E). Also featured are screening methods for identification of novel compds. that may be used to treat a viral disease. | | | |
| IT | 640281-90-9, Valopicitabine 640725-71-9, NM-283
1015079-99-8 1015080-00-8 1015080-23-5
1015080-28-0 1015080-31-5 1015080-38-2
1015080-56-4 1015080-58-6 1015080-59-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(compns. and methods for treatment of viral diseases) | | | |
| RN | 640281-90-9 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME) | | | |

Absolute stereochemistry. Rotation (+).



RN 640725-71-9 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



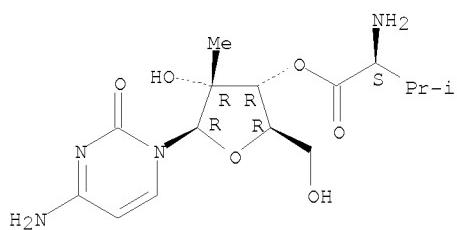
●2 HCl

RN 1015079-99-8 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2), mixt.
 with (3R,5aS,6R,8aS,9R,12S,12aR)-octahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyranolo[4,3-j]-1,2-benzodioxepin-10(3H)-one (CA INDEX NAME)

CM 1

CRN 640725-71-9
 CMF C15 H24 N4 O6 . 2 Cl H

Absolute stereochemistry. Rotation (+).

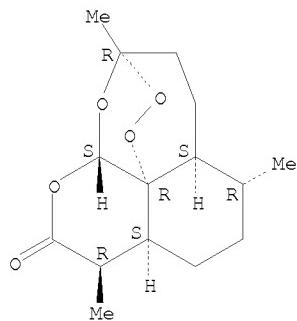


●2 HCl

CM 2

CRN 63968-64-9
 CMF C15 H22 O5

Absolute stereochemistry.



RN 1015080-00-8 CAPLUS

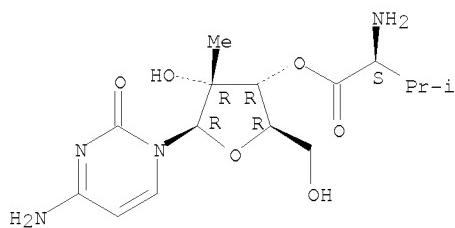
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2), mixt.
with 1,8,9-trihydroxy-3-methoxy-6H-benzofuro[3,2-c][1]benzopyran-6-one
(CA INDEX NAME)

CM 1

CRN 640725-71-9

CMF C15 H24 N4 O6 . 2 Cl H

Absolute stereochemistry. Rotation (+).

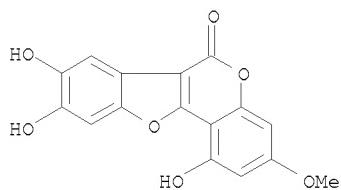


● 2 HCl

CM 2

CRN 524-12-9

CMF C16 H10 O7



RN 1015080-23-5 CAPLUS

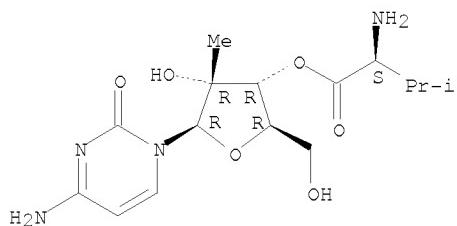
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2), mixt.
with (6E)-N-[(4-hydroxy-3-methoxyphenyl)methyl]-8-methyl-6-nonenamide (CA
INDEX NAME)

CM 1

CRN 640725-71-9

CMF C15 H24 N4 O6 . 2 Cl H

Absolute stereochemistry. Rotation (+).

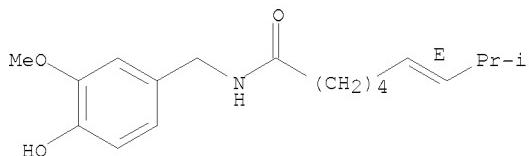


● 2 HCl

CM 2

CRN 404-86-4
CMF C18 H27 N O3

Double bond geometry as shown.

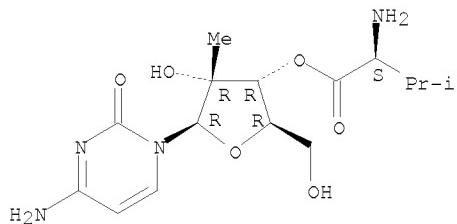


RN 1015080-28-0 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2), mixt.
 with 3-[(3,5-dibromo-4-hydroxyphenyl)methylene]-1,3-dihydro-5-iodo-2H-indol-2-one (CA INDEX NAME)

CM 1

CRN 640725-71-9
CMF C15 H24 N4 O6 . 2 Cl H

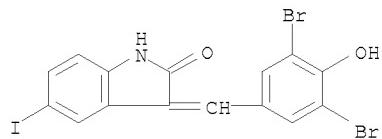
Absolute stereochemistry. Rotation (+).



● 2 HCl

CM 2

CRN 220904-83-6
CMF C15 H8 Br2 I N O2

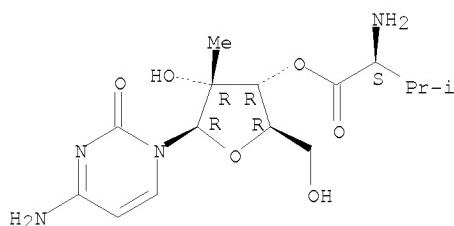


RN 1015080-31-5 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2), mixt.
 with 2,3,6,7-tetrahydro-9,10-dimethoxy-3-methyl-2-[(2,4,6-trimethylphenyl)imino]-4H-pyrimido[6,1-a]isoquinolin-4-one (CA INDEX NAME)

CM 1

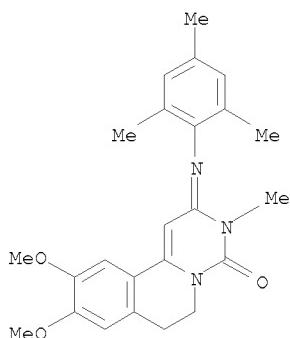
CRN 640725-71-9
 CMF C15 H24 N4 O6 . 2 Cl H

Absolute stereochemistry. Rotation (+).



● 2 HCl

CM 2

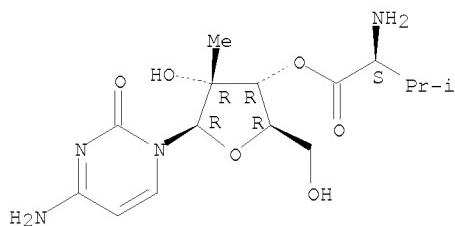
CRN 79855-88-2
 CMF C24 H27 N3 O3

RN 1015080-38-2 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2), mixt.
 with 2,3-dihydro-2-hydroxy-4H-1-benzopyran-4-one (CA INDEX NAME)

CM 1

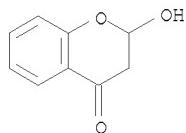
CRN 640725-71-9
 CMF C15 H24 N4 O6 . 2 Cl H

Absolute stereochemistry. Rotation (+).



● 2 HCl

CM 2

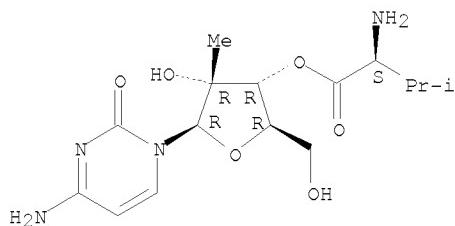
CRN 57669-32-6
CMF C9 H8 O3

RN 1015080-56-4 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2), mixt.
 with 1-(4-fluorophenyl)-4-[4-hydroxy-4-[3-(trifluoromethyl)phenyl]-1-piperidinyl]-1-butanone (CA INDEX NAME)

CM 1

CRN 640725-71-9
CMF C15 H24 N4 O6 . 2 Cl H

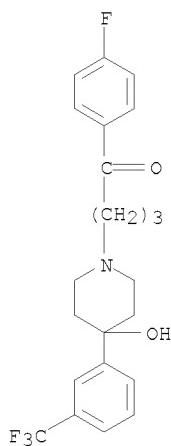
Absolute stereochemistry. Rotation (+).



● 2 HCl

CM 2

CRN 749-13-3
CMF C22 H23 F4 N O2

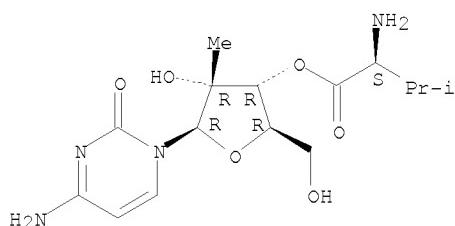


RN 1015080-58-6 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2), mixt.
 with 3-(2-phenyldiazenyl)-2,6-pyridinediamine (CA INDEX NAME)

CM 1

CRN 640725-71-9
 CMF C15 H24 N4 O6 . 2 Cl H

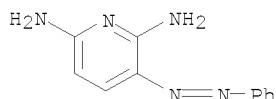
Absolute stereochemistry. Rotation (+).



● 2 HCl

CM 2

CRN 94-78-0
 CMF C11 H11 N5

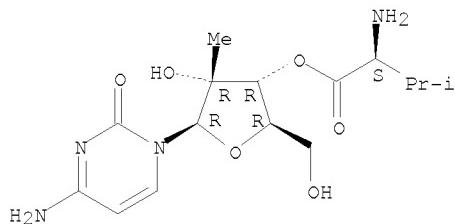


RN 1015080-59-7 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2), mixt.
 with α,α,α -trifluorothymidine (CA INDEX NAME)

CM 1

CRN 640725-71-9
 CMF C15 H24 N4 O6 . 2 Cl H

Absolute stereochemistry. Rotation (+).

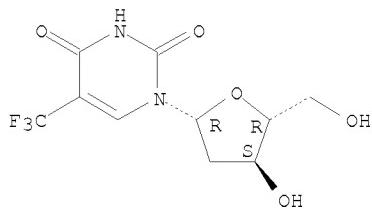


● 2 HCl

CM 2

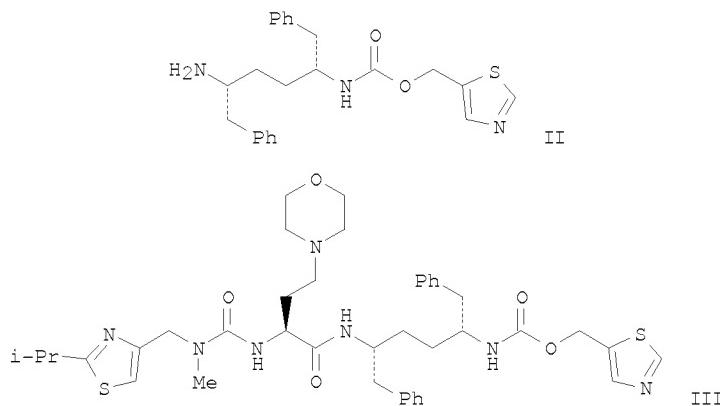
CRN 70-00-8
CMF C10 H11 F3 N2 O5

Absolute stereochemistry.



L11 ANSWER 4 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2008:90893 CAPLUS
 DN 148:192198
 TI Preparation of peptidomimetics as modulators of pharmacokinetic properties of therapeutics by inhibiting cytochrome P450 monooxygenase
 IN Desai, Manoj C.; Hong, Allen Yu; Liu, Hongtao; Xu, Lianhong; Vivian, Randall W.
 PA Gilead Sciences, Inc., USA
 SO PCT Int. Appl., 346pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------------|------|--|-----------------|--|
| PI WO 2008010921 | A2 | 20080124 | WO 2007-US15604 | 20070706 |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |
| US 20080108617 | A1 | 20080508 | US 2007-825605 | 20070706 |
| PRAI US 2006-819315P | P | 20060707 | | |
| US 2006-832371P | P | 20060721 | | |
| US 2007-903228P | P | 20070223 | | |
| OS MARPAT 148:192198 | | | | |
| GI | | | | |



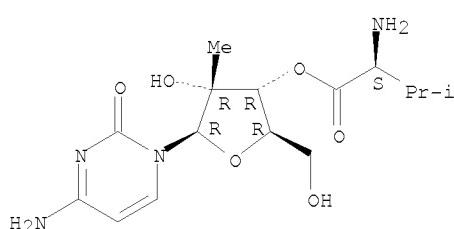
AB The invention is related to the preparation of R₈YZ₁[CONR₁(CR₂R₂)_m]nL₁NR₃CH[L₃A (L₄Ar)_p]CHR₄L₂CH[L₃A(L₄Ar)_p]NR₅COZ₂XR₉ [I; L₁ = C(R₆)₂, CO, SO₂, NHCO and derivs., OCO; R₄, R₆ = independently H, heteroalkyl, (un)substituted alkyl; L₂ = a covalent bond, C(R₆)₂, CO; each L₃ = independently a covalent bond, (un)substituted alkylene; each L₄ = L₃, O, CH₂O, NH; each A = H, (un)substituted alkyl, aryl, heterocyclyl with the proviso that when A = H, p = 0; Z₁, Z₂ = independently O, NH and derivs.; Y, X = independently heterocyclyl, heterocyclylalkyl; each Ar = independently (un)substituted (hetero)aryl; R₁, R₃, R₅ = independently H, (un)substituted arylhetero/hydroxy/amino/alkyl, alkylene-CO₂H, alkylene-CO-alkyl, etc.; R₈, R₉ are each one or more H's or substituents selected from Cl, CN, (un)substituted alkyl, aryl, heterocyclyl; m = 1-2; n = 0-1; each p = independently 0-1], their pharmaceutically acceptable salts, solvates and esters, and compns. containing them which improve the pharmacokinetics of a co-administered drug which is metabolized by cytochrome P 450 monooxygenase. Thus, a multi-step synthesis using 2-isopropyl-4-[(methylamino)methyl]-1,3-thiazole, (2S)-2-amino-4-[(tert-butoxycarbonyl)amino]butanoic acid Me ester, amine II and (BrCH₂CH₂)₂O was given for III. III inhibited CYP450 3A4 (IC₅₀ = 80-150 nM), CYP450 2C9 (IC₅₀ = 1,000-10,000 nM) and protease (EC50 > 20,000 nM in an anti HIV-1 cell culture assay). I alone or in combination with one or more addnl. therapeutic agents which are metabolized by cytochrome P 450 monooxygenase are useful for treating a viral infection, e.g. HIV (no data).

IT 640281-90-9, Valopicitabine 640725-71-9, NM-283
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. as modulators of pharmacokinetic properties of therapeutic agents)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

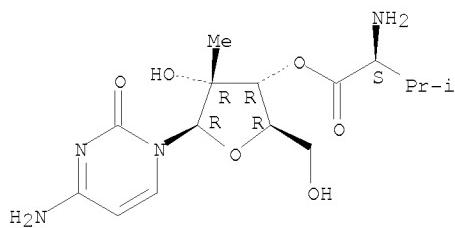
Absolute stereochemistry. Rotation (+).



RN 640725-71-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

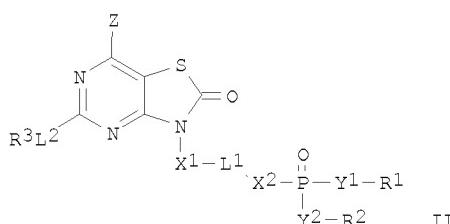
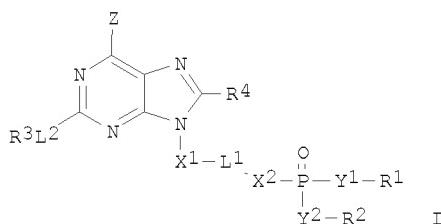
Absolute stereochemistry. Rotation (+).



● 2 HCl

L11 ANSWER 5 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2008:40914 CAPLUS
 DN 148:168504
 TI Preparation of purine and thiadeazapurine phosphonate derivatives as modulators of toll-like receptor 7
 IN Chong, Lee S.; Desai, Manoj C.; Gallagher, Brian; Graupe, Michael; Halcomb, Randall L.; Yang, Hong; Zhang, Jennifer R.
 PA Gilead Sciences, Inc., USA
 SO PCT Int. Appl., 273pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2008005555 | A1 | 20080110 | WO 2007-US15615 | 20070706 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA,
CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG,
KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL,
PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | US 20080008682 | A1 | 20080110 | US 2007-825377 | 20070706 |
| PRAI | US 2006-819490P | P | 20060707 | | |
| | US 2006-832851P | P | 20060724 | | |
| OS | MARPAT 148:168504 | | | | |
| GI | | | | | |



AB The present application provides for a compound I [Z = OH, NH₂; X₁ = (un)substituted alkylene, alkenylene, alkynylene, carbocyclylene, heterocyclylene; L₁ = bond, (un)substituted arylene, heterocyclylene, carbocyclylene, S, S(:O), SO₂, NR₅, O; X₂ = bond, (un)substituted alkylene; L₂ = NR₅, NR₅C(:O), O, S, S(:O), SO₂, bond; R₃ = H, (un)substituted alkyl, heteroalkyl, alkenyl, aryl, arylalkyl, heterocycl, heterocyclalkyl, Y₁, Y₂ = bond, O, NR₅, Y₁R₁, Y₂R₂ = ON:CR₆R₇; R₁, R₂ = H, (un)substituted alkyl, carbocyclyl, heterocyclyl, alkenyl, alkynyl, arylalkyl, etc.; R₄ = H, halogen, OH, O-alkyl, O-alkylene-OCO₂R₅, OCO₂R₅, SH, NHR₅; R₅, R₆, R₇ = H, (un)substituted alkyl, carbocyclyl, heterocycl, alkenyl, alkynyl, arylalkyl, heterocyclalkyl, etc.] or II or a pharmaceutically acceptable salt, solvate, and/or ester thereof, compns. containing such compds., therapeutic methods that include the administration of such compds., and therapeutic methods that include the administration of such compds. with at least one addnl. active agent. Thus, [(3-((6-amino-8-hydroxy-2-(2-methoxyethoxy)-9H-purin-9-yl)methyl)phenyl)methyl](methyl)phosphinic acid [I; Z = NH₂, R₄ = OH, L₂ = O, R₃ = CH₂CH₂OMe, X₁ = X₂ = CH₂, L₁ = 1,3-phenylene, Y₁R₁ = Me, Y₂R₂ = OH] was prepared from 6-chloroadenine via N-alkylation with 3-(BrCH₂)C₆H₄CO₂Me, alkoxylation with MeOCH₂CH₂OH, reesterification with MeI, bromination with Br₂, Dibal-H reduction, methanolysis with NaOMe/MeOH, acid hydrolysis, bromination with PBr₃, phosphorylation with MeP(OEt)₂ and acid hydrolysis under microwave irradiation. The toll-like receptor 7 modulating activity of I and II were investigated (no data).

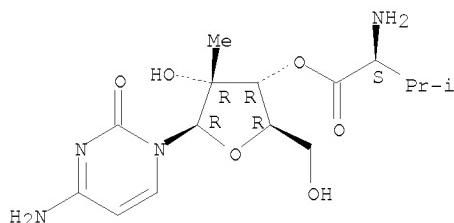
IT 640281-90-9, Valopicitabine 640725-71-9, NM-283

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. as modulators of Toll-like receptor 7 useful in combination therapy and prevention of TLR7 activation-related diseases)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

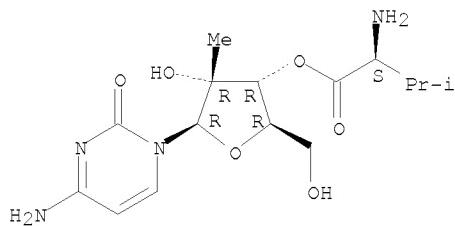
Absolute stereochemistry. Rotation (+).



RN 640725-71-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA
INDEX NAME)

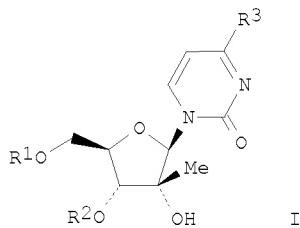
Absolute stereochemistry. Rotation (+).



● 2 HCl

L11 ANSWER 6 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2007:1332915 CAPLUS
 DN 148:11439
 TI 2'-C-Methyl-Ribofuranosyl Cytidine Prodrugs, Pharmaceutical Compositions
and Uses Thereof
 IN Gallop, Mark A.
 PA USA
 SO U.S. Pat. Appl. Publ., 59pp.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------------|------|----------|-----------------|----------|
| PI US 20070270374 | A1 | 20071122 | US 2007-752214 | 20070522 |
| PRAI US 2006-808360P | P | 20060522 | | |
| OS MARPAT 148:11439 | | | | |
| GI | | | | |



AB The present disclosure provides the preparation of 2'-C-methyl-ribofuranosyl cytidine prodrugs I, wherein R¹ and R² are independently H, acyl, acyloxyalkylcarbonyl, oxycarbonyl, substituted aminocarbonyl; R³ is substituted imine, substituted amine, and pharmaceutical compns. thereof to treat viral diseases such as hepatitis C. Thus, β-(4-allyloxycarbonylamino-2-oxo-1H-pyrimidin-1-yl)-2-C-methylribofuranose was prepared (no data) and tested in vitro in combination with antiviral agents to treat viral diseases, wherein the second antiviral agent is selected from an interferon, ribavirin, interleukin, an NS3 protease inhibitor, cysteine protease inhibitor, thiazolidine derivative, thiazolidine, benzanilide, phenanthrenequinone, a helicase inhibitor, a polymerase inhibitor, a nucleotide analog, gliotoxin, cerulenin, antisense phosphorothioate oligodeoxyribonucleotides, inhibitor of IRES-dependent translation, and a ribozyme. In vitro compound transport assays with CNT1, CNT2, CNT3, ENT1 and ENT2 expressing cells, are claimed.

IT 957687-30-8P 957687-34-2P 957687-53-5P
 957687-55-7P 957687-58-0P 957687-62-6P
 957687-64-8P 957687-83-1P

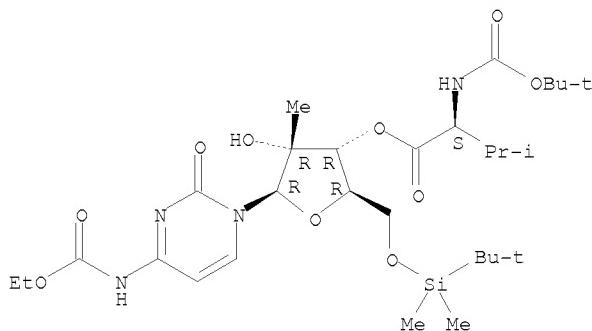
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(2'-C-methyl-ribofuranosyl cytidine prodrugs, pharmaceutical compns. and uses thereof)

RN 957687-30-8 CAPLUS

CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with 5'-O-[(1,1-dimethylethyl)dimethylsilyl]-N-(ethoxycarbonyl)-2'-C-methylcytidine (CA INDEX NAME)

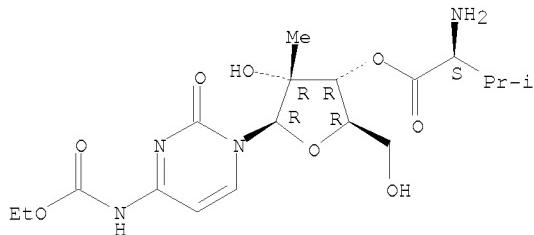
Absolute stereochemistry.



RN 957687-34-2 CAPLUS

CN L-Valine, 3'-ester with N-(ethoxycarbonyl)-2'-C-methylcytidine (CA INDEX NAME)

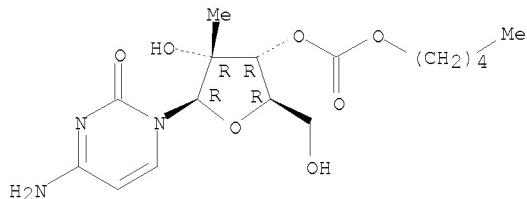
Absolute stereochemistry.



RN 957687-53-5 CAPLUS

CN Cytidine, 2'-C-methyl-, 3'-(pentyl carbonate) (CA INDEX NAME)

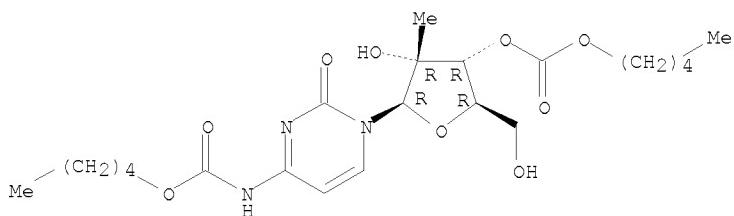
Absolute stereochemistry.



RN 957687-55-7 CAPLUS

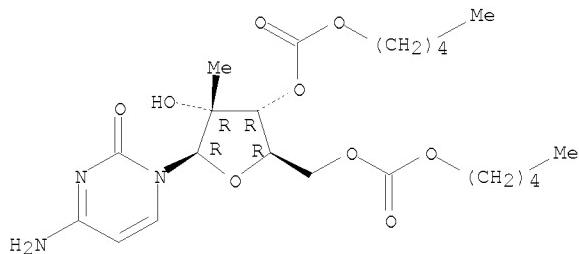
CN Cytidine, 2'-C-methyl-N-[(pentyloxy)carbonyl]-, 3'-(pentyl carbonate) (CA INDEX NAME)

Absolute stereochemistry.



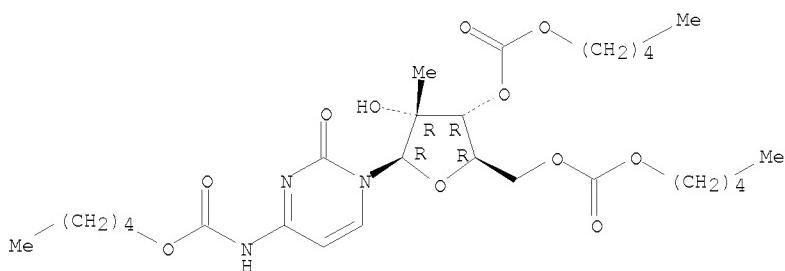
RN 957687-58-0 CAPLUS
 CN Cytidine, 2'-C-methyl-, 3',5'-bis(pentyl carbonate) (CA INDEX NAME)

Absolute stereochemistry.



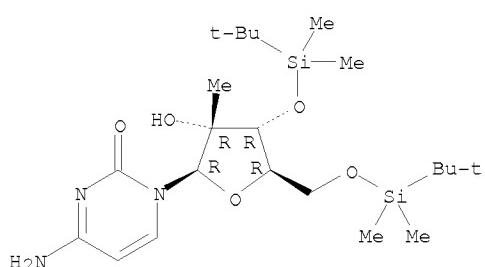
RN 957687-62-6 CAPLUS
 CN Cytidine, 2'-C-methyl-N-[(pentyloxy)carbonyl]-, 3',5'-bis(pentyl carbonate) (CA INDEX NAME)

Absolute stereochemistry.



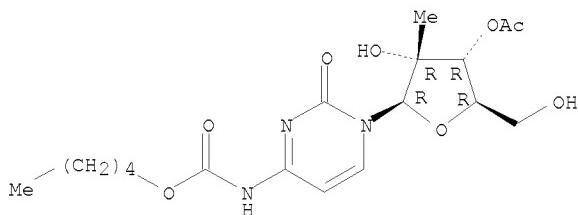
RN 957687-64-8 CAPLUS
 CN Cytidine, 3',5'-bis-O-[(1,1-dimethylethyl)dimethylsilyl]-2'-C-methyl- (CA INDEX NAME)

Absolute stereochemistry.



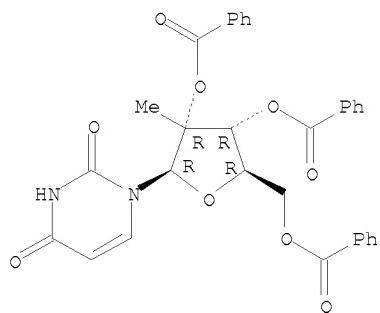
RN 957687-83-1 CAPLUS
 CN Cytidine, 2'-C-methyl-N-[(pentyloxy)carbonyl]-, 3'-acetate (CA INDEX NAME)

Absolute stereochemistry.



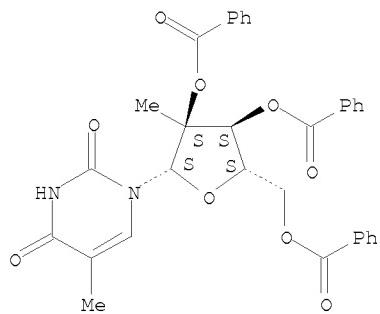
L11 ANSWER 7 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2007:1164795 CAPLUS
 DN 147:534049
 TI 2'-C-methyl branched pyrimidine ribonucleoside analogues: potent inhibitors of RNA virus replication
 AU Benzaria, Samira; Bardiot, Dorothee; Bouisset, Tony; Counor, Clement; Rabeson, Celine; Pierra, Claire; Storer, Richard; Loi, Anna Giulia; Cadeddu, Alessandra; Mura, Massimo; Musiu, Chiara; Liuzzi, Michel; Loddo, Roberta; Bergelson, Svetlana; Bichko, Vadim; Bridges, Edward; Cretton-Scott, Erika; Mao, John; Sommadossi, Jean-Pierre; Seifer, Maria; Standring, David; Tausek, Michele; Gosselin, Gilles; La Colla, Paolo
 CS Laboratoire Coopératif Idenix-CNRS-Université Montpellier II, Montpellier, Fr.
 SO Antiviral Chemistry & Chemotherapy (2007), 18(4), 225-242
 CODEN: ACCHEH; ISSN: 0956-3202
 PB International Medical Press, Ltd.
 DT Journal
 LA English
 OS CASREACT 147:534049
 AB RNA viruses are the agents of numerous wide-spread and often severe diseases. Their unique RNA-dependent RNA polymerase (RDRP) is essential for replication and, thus, constitutes a valid target for the development of selective chemotherapeutic agents. In this regard, the authors have investigated sugar-modified ribonucleoside analogs as potential inhibitors of the RDRP. Title compds. retain 'natural' pyrimidine bases, but possess a β -Me substituent at the 2'-position of the D- or L-ribose moiety. Evaluation against a broad range of RNA viruses, either single-stranded pos. (ssRNA+), single-stranded neg. (ssRNA-) or double-stranded (dsRNA), revealed potent activities for D-2'-C-methyl-cytidine and -uridine against ssRNA+, and dsRNA viruses. None of the L-enantiomers were active. Moreover, the 5'-triphosphates of the active D-enantiomers were found to inhibit the bovine virus diarrhea virus polymerase. Thus, the 2'-Me branching of natural pyrimidine ribonucleosides transforms physiol. mols. into potent, broad-spectrum antiviral agents that merit further development.
 IT 23643-36-9P 957535-48-7P 957535-51-2P
 957535-53-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (pyrimidine ribonucleoside analogs as potent inhibitors of RNA virus replication)
 RN 23643-36-9 CAPLUS
 CN 2,4(1H,3H)-Pyrimidinedione, 1-(2,3,5-tri-O-benzoyl-2-C-methyl- β -D-ribofuranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



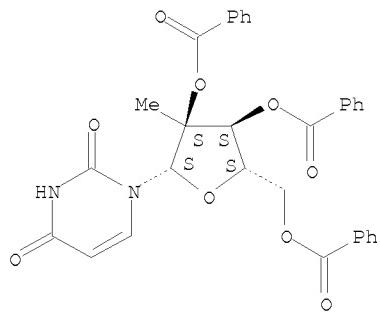
RN 957535-48-7 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-methyl-1-(2,3,5-tri-O-benzoyl-2-C-methyl-
β-L-ribofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



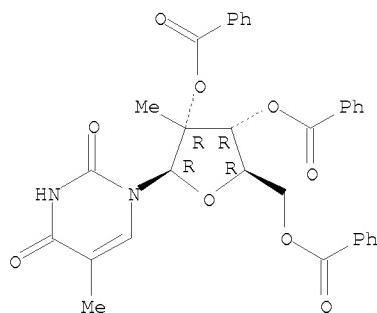
RN 957535-51-2 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2,3,5-tri-O-benzoyl-2-C-methyl-β-L-
ribofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 957535-53-4 CAPLUS
CN Uridine, 5-methyl-2'-C-methyl-, 2',3',5'-tribenzoate (CA INDEX NAME)

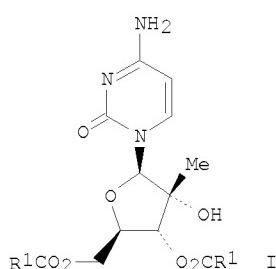
Absolute stereochemistry.



RE.CNT 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2007:1121524 CAPLUS
 DN 147:407046
 TI Preparation of nucleosides as Hepatitis C virus NS5b polymerase inhibitors and antiviral agents via regioselective O-acylation reaction
 IN Sarma, Keshab
 PA Roche Palo Alto LLC, USA
 SO U.S. Pat. Appl. Publ., 15pp.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|--|-----------------|----------|
| PI US 20070232562 | A1 | 20071004 | US 2007-732983 | 20070404 |
| WO 2007113159 | A1 | 20071011 | WO 2007-EP52866 | 20070326 |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | | |
| | RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | |
| PRAI US 2006-789491P | P | 20060404 | | |
| OS CASREACT 147:407046; MARPAT 147:407046 | | | | |
| GI | | | | |



AB Nucleosides I, wherein R1 is Compds. having the formula I wherein R1 is C2-5 (un)-branched alkyl, C2-5 (un)-branched alkenyl, C3-5 cycloalkyl, C2-5 lower halo-alkyl, were prepared as Hepatitis C

virus NS5b polymerase inhibitors. Also disclosed are compns. and methods for inhibiting hepatitis replication, processes for making the compds. and synthetic intermediates used in the process. Thus, nucleoside I.HCl [R1 = C(O)Et] was prepared in 60% yield by regioselective O-acylation of I (R1 = H) with propionyl chloride. Title compds. were tested in vivo as Hepatitis C virus NS5b polymerase inhibitors and antiviral agents (a dose of between 1.0 and 6.0 g per day is administered to the patient). Determination of pharmacokinetic parameters of title nucleosides in rats, is reported.

IT 951131-56-9P 951131-58-1P 951131-60-5P

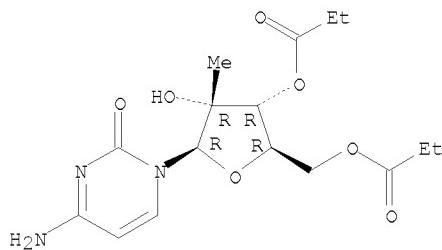
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nucleosides as Hepatitis C virus NS5b polymerase inhibitors and antiviral agents via regioselective O-acylation reaction)

RN 951131-56-9 CAPLUS

CN Cytidine, 2'-C-methyl-, 3',5'-dipropanoate, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.

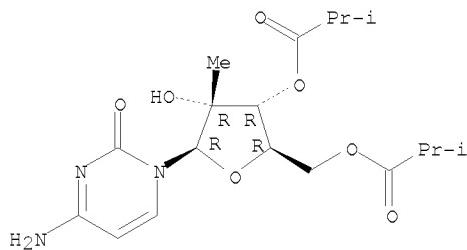


● HCl

RN 951131-58-1 CAPLUS

CN Cytidine, 2'-C-methyl-, 3',5'-bis(2-methylpropanoate), hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.

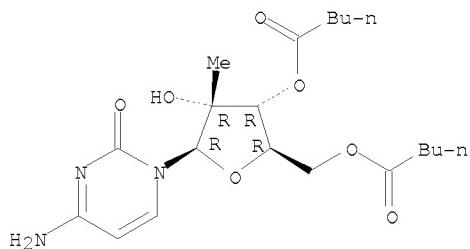


● HCl

RN 951131-60-5 CAPLUS

CN Cytidine, 2'-C-methyl-, 3',5'-dipentanoate, hydrochloride (1:1) (CA INDEX NAME)

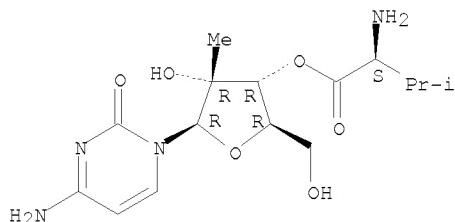
Absolute stereochemistry.



● HCl

IT 640281-90-9
 RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (preparation of nucleosides as Hepatitis C virus NS5b polymerase inhibitors and antiviral agents via regioselective O-acylation reaction)
 RN 640281-90-9 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



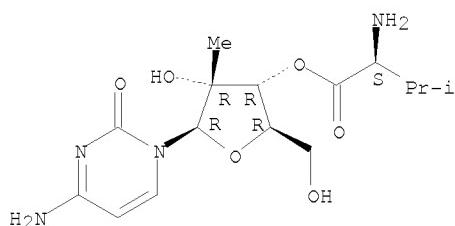
L11 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2007:1112011 CAPLUS
 DN 147:514184
 TI New therapies for hepatitis C
 AU Modi, Apurva A.; Hoofnagle, Jay H.
 CS Liver Diseases Branch, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, USA
 SO Hepatology (Hoboken, NJ, United States) (2007), 46(3), 615-617
 CODEN: HPTLD9; ISSN: 0270-9139
 PB John Wiley & Sons, Inc.
 DT Journal; General Review
 LA English
 AB A review. The research Forestier et al. (2007) entitled "Antiviral activity of telaprevir (VX-950) and peginterferon alfa-2a in patients with hepatitis C" is reviewed with commentary and refs. Forestier and her coinvestigators from Saarland University Hospital, the University of Amsterdam, and Vertex Pharmaceuticals describe the preliminary clin. results of a small phase 1b trial of telaprevir. The report provides information on HCV RNA and alanine aminotransferase levels in 8 patients who received telaprevir alone, 8 who received telaprevir with peginterferon, and 4 who served as controls and received peginterferon alone for 2 wk. Telaprevir was then stopped, but the patients were offered a continuation of treatment with a combination of peginterferon and ribavirin until 48 wk and thus were provided the standard of care for chronic hepatitis C, genotype 1. Telaprevir led to a rapid decline in HCV RNA levels within 1-4 days. The combination of peginterferon with telaprevir resulted in a similar early decline in viral levels, but importantly, the combination therapy was associated with an addnl., continuing decline after the first 4 days of treatment.
 IT 640281-90-9, Valopicitabine
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
 (valopicitabine, BILN-2061 showed greater toxicity hence were abandoned
 from usage by patient with hepatitis C)

RN 640281-90-9 CAPLUS

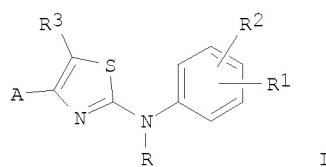
CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

| | | | | |
|---------|--|--|----------|-----------------|
| L11 | ANSWER 10 OF 37 CAPLUS | COPYRIGHT 2008 ACS on STN | | |
| AN | 2007:1029651 CAPLUS | | | |
| DN | 147:365486 | | | |
| TI | Preparation of 2-(phenylamino)thiazole derivatives as inhibitors of viral replication for the treatment of hepatitis C infection | | | |
| IN | Zhang, Suoming; Phadke, Avinash; Wang, Xiangzhu; Liu, Cuixian | | | |
| PA | Achillion Pharmaceuticals, Inc., USA | | | |
| SO | PCT Int. Appl., 134pp. | | | |
| | CODEN: PIXXD2 | | | |
| DT | Patent | | | |
| LA | English | | | |
| FAN.CNT | 1 | | | |
| | PATENT NO. | KIND | DATE | APPLICATION NO. |
| ----- | ----- | ----- | ----- | ----- |
| PI | WO 2007103550 | A2 | 20070913 | WO 2007-US6023 |
| | WO 2007103550 | A3 | 20071108 | 20070308 |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, GT, HN, HR, ID, IL, IN, IS, JP, KE, KG, KM, KN,
KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN,
MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS,
RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | | |
| | RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA | | |
| | US 20070213301 | A1 | 20070913 | US 2007-683749 |
| PRAI | US 2006-780609P | P | 20060308 | 20070308 |
| OS | MARPAT 147:365486 | | | |
| GI | | | | |



AB Title compds. I [wherein A = (un)substituted Ph, benzyl, heteroaryl, etc.; R = CHO, C(O)COOH, C(O)CONH₂, etc.; R1 = (un)substituted haloalkyl, haloalkoxy, alkylamino, etc.; R2 (0-2 substituents) = halo, OH, amino, etc.; R3 = H, halo, OH, etc.] and pharmaceutically acceptable salts thereof were prepared as inhibitors of viral replication. For instance, cyclocondensation of 3-bromoacetylpyridine with N-(4-pentoxy-3-trifluoromethylphenyl)thiourea followed by acylation of the resultant anilinothiazole with acetyl chloride gave II. This product showed inhibition of HCV replication with an EC₅₀ of < 1 μM. Therefore, the invented compds. and their pharmaceutical compns. are useful for the treatment of hepatitis C infection.

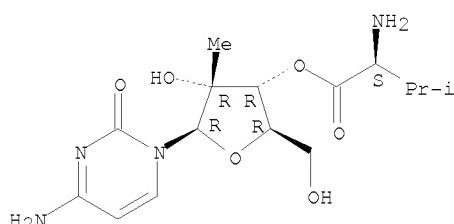
IT 640281-90-9, Valopicitabine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (co-drug; preparation of (phenylamino)thiazoles as inhibitors of viral replication for treatment of hepatitis C infection)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L11 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2007:618644 CAPLUS

DN 147:31277

TI Polycyclic phenolic compounds and use in treating viral infections

IN Dugourd, Dominique

PA Migenix Corporation, Can.

SO PCT Int. Appl., 77pp.

CODEN: PIXD2

DT Patent

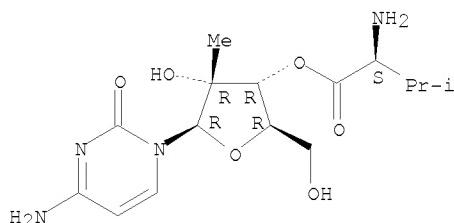
LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------|--|------|---|-----------------|----------|
| PI | WO 2007062528 | A1 | 20070607 | WO 2006-CA1965 | 20061201 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, | | |

KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,
 MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS,
 RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ,
 UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
 CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
 GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
 AU 2006299426 A1 20070412 AU 2006-299426 20061002
 US 20070173440 A1 20070726 US 2006-542930 20061002
 PRAI US 2005-722679P P 20050930
 US 2006-787549P P 20060329
 WO 2006-US38823 W 20061002
 OS MARPAT 146:395250
 AB This invention relates to 3-ether or 3-thioether derivs. of cyclosporin or a pharmaceutically acceptable salt or solvate thereof, in combination with a second therapeutic agent for sequential or simultaneous administration in treatment and prevention of hepatitis C viral (HCV) infection. The second therapeutic agent is selected from modulators of NS3-4A protease, modulators of NS5B RNA-dependent RNA polymerase, and immunomodulatory agents. Thus, treatment of 1,4-diacetyl-3-methoxy-4-(gamma-hydroxymethylleucine)cyclosporin (275 mg) in methanol with 25 weight% sodium methoxide in methanol at room temperature yielded 33 mg of 3-methoxy-4-(gamma-hydroxymethylleucine)cyclosporin (Compound T). The Compound T potently inhibited HCV replication in human liver cells to a greater extent than cyclosporin used as a control. In addition, when considering the level of cytotoxicity, the compound exhibited a wider safety margin (for example, cytotoxicity IC₅₀ vs. antiviral EC₅₀) than cyclosporine. The combination of Compound T and interferon- α was additive.
 IT 640281-90-9, Valopicitabine
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cyclosporin derivs. and their combinations for treatment and prevention of hepatitis C infection)
 RN 640281-90-9 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

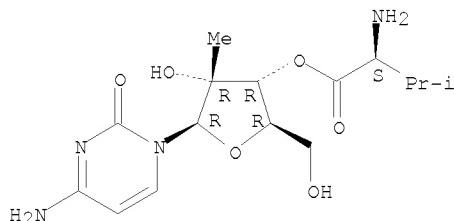


L11 ANSWER 13 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2007:320324 CAPLUS
 DN 146:394149
 TI Valopicitabine dihydrochloride: a specific polymerase inhibitor of hepatitis C virus
 AU Toniutto, Pierluigi; Fabris, Carlo; Bitetto, Davide; Fornasiere, Ezio;
 Rapetti, Rachele; Pirisi, Mario
 CS Internal Medicine, Medical Liver Transplantation Unit, DPMSC, University
 of Udine, Udine, 33100, Italy
 SO Current Opinion in Investigational Drugs (Thomson Scientific) (2007),
 8(2), 150-158
 CODEN: COIDAZ; ISSN: 1472-4472
 PB Thomson Scientific
 DT Journal; General Review
 LA English
 AB A review. Idenix Pharmaceuticals Inc and Novartis AG are codeveloping valopicitabine dihydrochloride, a once-daily oral nucleoside for the potential treatment of HCV infection. In Jan. 2005, a phase IIa clin. trial comparing valopicitabine dihydrochloride with pegylated IFN in

treatment-naive HCV patients was ongoing, in addition to a phase IIb trial in patients that had previously failed pegylated IFN and ribavirin combination therapy. In Jan. 2006, an international phase III trial in treatment-refractory patients was planned for the first half of the year, with a phase III trial in treatment-naive individuals planned for the second half of the year.

- IT 640725-71-9, Valopicitabine dihydrochloride
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (valopicitabine dihydrochloride and interferon or ribavirin combination therapy was used to treat patient with hepatitis C virus infection)
- RN 640725-71-9 CAPLUS
- CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

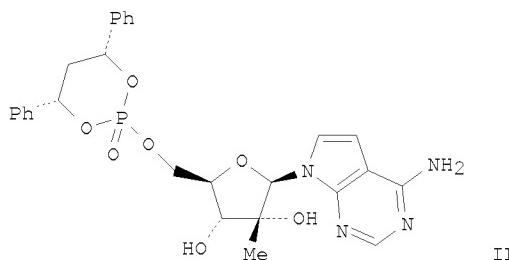
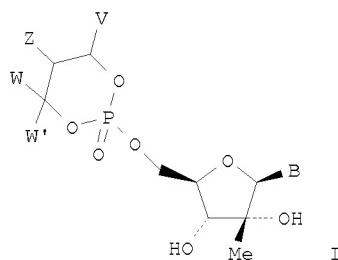


● 2 HCl

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L11 ANSWER 14 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2007:200728 CAPLUS
 DN 146:274570
 TI Preparation of 2'-C-Me nucleoside 5'-monophosphate and 4'-C-Me nucleoside 5'-monophosphate prodrugs for the treatment of hepatitis C viral infection
 IN Erion, Mark D.; Reddy, K. Raja; MacCoss, Malcolm; Olsen, David B.
 PA Merck & Co., Inc., USA; Metabasis Therapeutics, Inc.
 SO PCT Int. Appl., 268pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1
- | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------------|--|----------|-----------------|----------|
| WO 2007022073 | A2 | 20070222 | WO 2006-US31614 | 20060814 |
| WO 2007022073 | A3 | 20071115 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | | | |
| RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA | | | |
| AU 2006279720 | A1 | 20070222 | AU 2006-279720 | 20060814 |
| CA 2618713 | A1 | 20070222 | CA 2006-2618713 | 20060814 |
| EP 1915053 | A2 | 20080430 | EP 2006-801410 | 20060814 |
| R: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS | | | |
| PRAI US 2005-707767P | P | 20050812 | | |

US 2006-772649P P 20060213
 WO 2006-US31614 W 20060814
 OS MARPAT 146:274570
 GI



AB 2'-C-Me nucleoside 5'-monophosphate and 4'-C-Me nucleoside 5'-monophosphate prodrugs I, wherein B can be heterocyclic or heteroaryl rings; V is an optionally substituted monocyclic aryl or heteroaryl ring; W and W' are independently (un)substituted monocyclic aryl or heteroaryl rings, alkyl, aryl, heterocycloaryl or aralkyl groups; Z is halo, cyano, keto, amido, etc. are prepared. Further, I can also be prepared such that V and Z are connected via 3-5 atoms to form a cyclic group fused to aryl groups; Z and W connected via 3-5 atoms to form a cyclic group containing one heteroarom; or W and W' connected via an addnl. 2-5 atoms to form a cyclic group optionally containing 0-2 heteroatoms. Thus, II was prepared and tested for its in vitro activation in human liver microsomes by product capture (0.044 nmol/mg/min at activation 250 μ M). I were also tested for their NTP accumulation in hepatocytes; in HCV-infected human liver assays; for tissue distribution following oral administration and the oral bioavailability in normal male rats.

IT
 926655-64-3P 926655-66-5P 926655-67-6P
 926655-68-7P 926655-69-8P 926655-73-4P
 926655-74-5P 926655-75-6P 926655-76-7P
 926655-77-8P 926655-78-9P 926655-80-3P

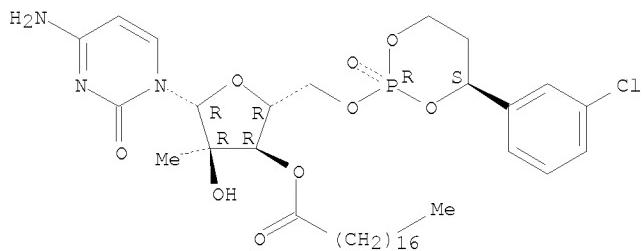
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2'-C-Me nucleoside 5'-monophosphate and 4'-C-Me nucleoside 5'-monophosphate prodrugs for the treatment of hepatitis C viral infection)

RN 926655-64-3 CAPLUS

CN Cytidine, 5'-O-[(2R,4S)-4-(3-chlorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-, 3'-octadecanoate (CA INDEX NAME)

Absolute stereochemistry.



RN 926655-66-5 CAPLUS

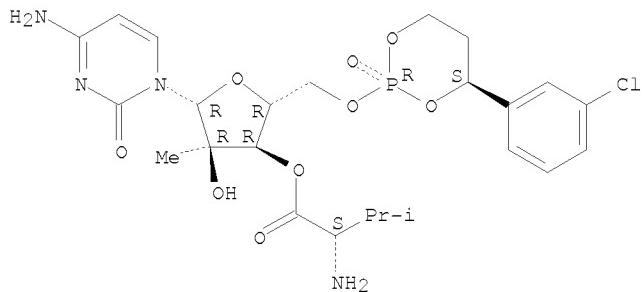
CN L-Valine, 3'-ester with 5'-O-[(2R,4S)-4-(3-chlorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methylcytidine, 2,2,2-trifluoroacetate (1:?)
(CA INDEX NAME)

CM 1

CRN 926655-65-4

CMF C24 H32 Cl N4 O9 P

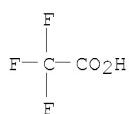
Absolute stereochemistry.



CM 2

CRN 76-05-1

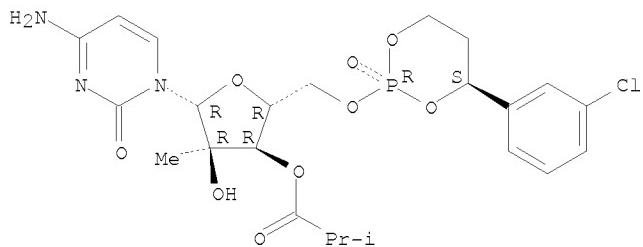
CMF C2 H F3 O2



RN 926655-67-6 CAPLUS

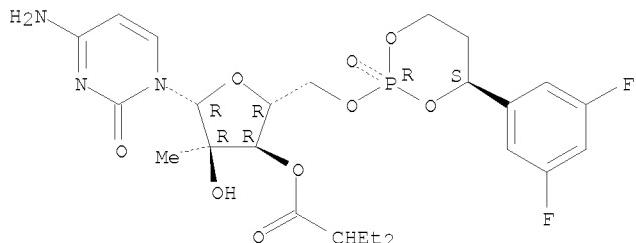
CN Cytidine, 5'-O-[(2R,4S)-4-(3-chlorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-, 3'-(2-methylpropanoate) (CA INDEX NAME)

Absolute stereochemistry.



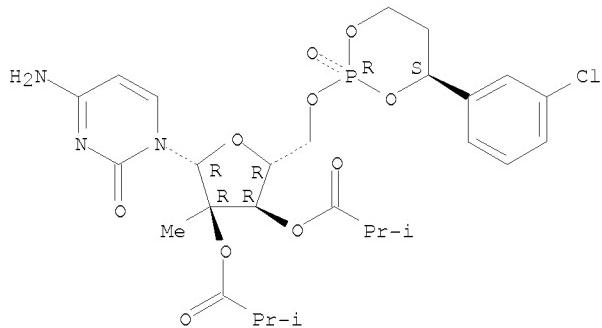
RN 926655-68-7 CAPLUS
 CN Cytidine, 5'-O-[(2R,4S)-4-(3,5-difluorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-, 3'-(2-ethylbutanoate) (CA INDEX NAME)

Absolute stereochemistry.



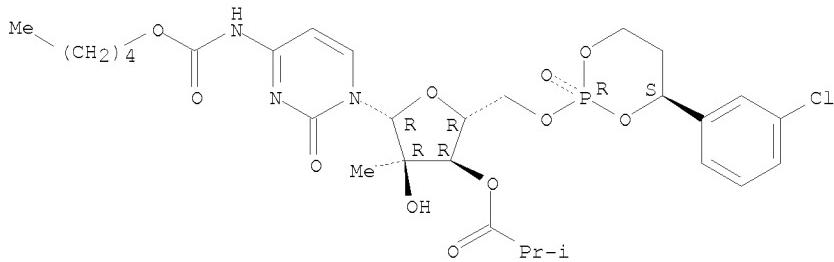
RN 926655-69-8 CAPLUS
 CN Cytidine, 5'-O-[(2R,4S)-4-(3-chlorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-, 2',3'-bis(2-methylpropanoate) (CA INDEX NAME)

Absolute stereochemistry.



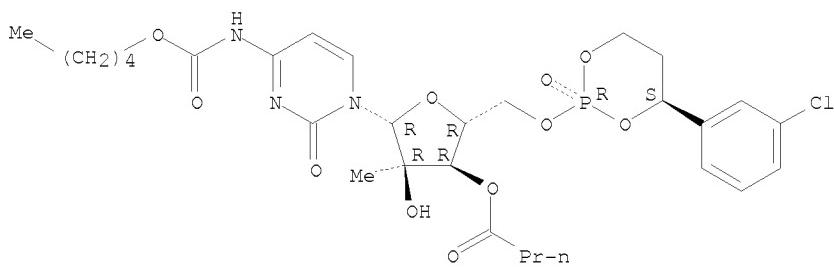
RN 926655-73-4 CAPLUS
 CN Cytidine, 5'-O-[(2R,4S)-4-(3-chlorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-N-[(pentyloxy)carbonyl]-, 3'-(2-methylpropanoate) (CA INDEX NAME)

Absolute stereochemistry.



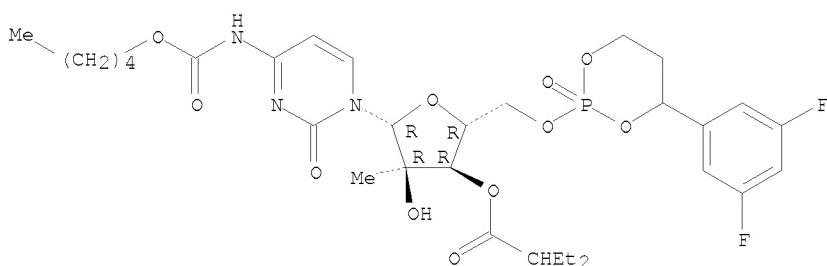
RN 926655-74-5 CAPLUS
 CN Cytidine, 5'-O-[(2R,4S)-4-(3-chlorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-N-[(pentyloxy)carbonyl]-, 3'-butanoate (CA INDEX NAME)

Absolute stereochemistry.



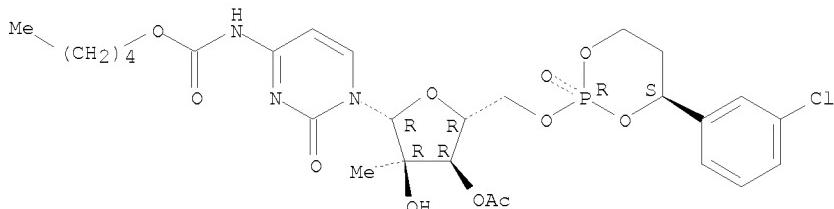
RN 926655-75-6 CAPLUS
 CN Cytidine, 5'-O-[4-(3,5-difluorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-N-[(pentyloxy)carbonyl]-, 3'-(2-ethylbutanoate) (CA INDEX NAME)

Absolute stereochemistry.



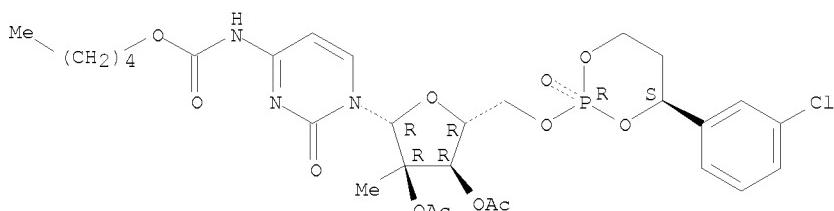
RN 926655-76-7 CAPLUS
 CN Cytidine, 5'-O-[(2R,4S)-4-(3-chlorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-N-[(pentyloxy)carbonyl]-, 3'-acetate (CA INDEX NAME)

Absolute stereochemistry.



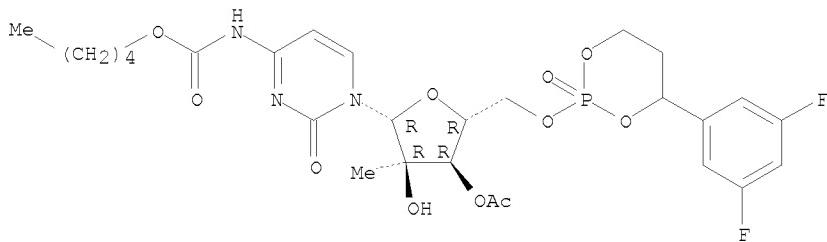
RN 926655-77-8 CAPLUS
 CN Cytidine, 5'-O-[(2R,4S)-4-(3-chlorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-N-[(pentyloxy)carbonyl]-, 2',3'-diacetate (CA INDEX NAME)

Absolute stereochemistry.



RN 926655-78-9 CAPLUS
 CN Cytidine, 5'-O-[4-(3,5-difluorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-N-[(pentyloxy)carbonyl]-, 3'-acetate (CA INDEX NAME)

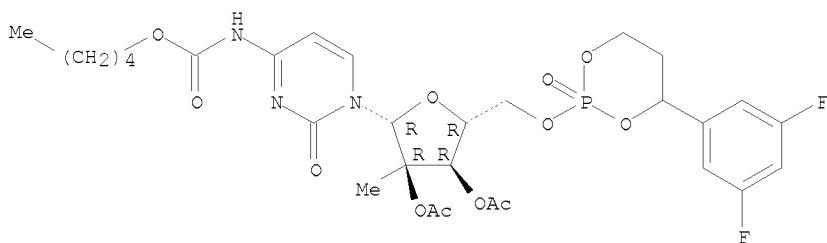
Absolute stereochemistry.



RN 926655-80-3 CAPLUS

CN Cytidine, 5'-O-[4-(3,5-difluorophenyl)-2-oxido-1,3,2-dioxaphosphorinan-2-yl]-2'-C-methyl-N-[(pentyloxy)carbonyl]-, 2',3'-diacetate (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 15 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2007:85871 CAPLUS

DN 146:177157

TI Small animal model for HCV replication

IN Weiner, Amy; Aukerman, Sharon Lea; Mendel, Dirk; Zhu, Qing

PA Novartis A.-G., Switz.

SO PCT Int. Appl., 85pp.

CODEN: PIXD2

DT Patent

LA English

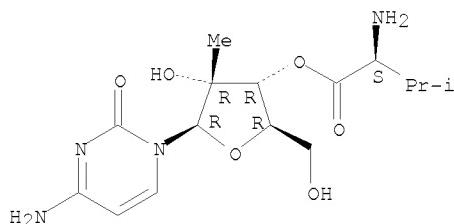
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|--|----------|-----------------|----------|
| PI | WO 2007011777 | A2 | 20070125 | WO 2006-US27485 | 20060715 |
| | WO 2007011777 | A3 | 20071011 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | | | |
| | RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA | | | |
| | CA 2615626 | A1 | 20070125 | CA 2006-2615626 | 20060715 |
| | EP 1909564 | A2 | 20080416 | EP 2006-787397 | 20060715 |
| | R: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS | | | |
| PRAI | US 2005-700475P | P | 20050718 | | |
| | US 2006-776640P | P | 20060223 | | |
| | WO 2006-US27485 | W | 20060715 | | |
| AB | An animal model for HCV (hepatitis C virus) replication and/or production of virus or virus like particles is provided. The invention utilizes an HCV replicon present in a cell to | | | | |

deliver HCV nucleic acid and replicate and express HCV proteins in an animal model comprising an animal that has been immunocompromised. The invention further provides a method of treatment or prevention of HCV in a mammal which comprises administering to the mammal a combination which comprises an immunomodulatory compound and another antiviral agent. Also provided are cell lines showing a decreased sensitivity to interferon alpha or some other immunomodulator and methods of making or isolating such cell lines.

IT 640281-90-9, Valopicitabine
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (small animal model for hepatitis C virus replication)
 RN 640281-90-9 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L11 ANSWER 16 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2006:1283521 CAPLUS
 DN 146:20343
 TI Use of 4-[3,5-Bis-(2-hydroxyphenyl)-[1,2,4]-triazol-1-yl]benzoic acid for the treatment of liver diseases in which iron plays a role in pathogenesis
 IN Alberti, Daniele; Marks, Peter; Nick, Hanspeter; Rojkjaer, Lisa Grace
 PA Novartis AG, Switz.; Novartis Pharma GmbH
 SO PCT Int. Appl., 20pp.
 CODEN: PIXXD2

DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-----------------|--|----------|------------------|----------|
| PI | WO 2006130532 | A2 | 20061207 | WO 2006-US20677 | 20060530 |
| | WO 2006130532 | A3 | 20071122 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| | RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA | | | |
| AU | 2006252718 | A1 | 20061207 | AU 2006-252718 | 20060530 |
| CA | 2608709 | A1 | 20061207 | CA 2006-2608709 | 20060530 |
| EP | 1893198 | A2 | 20080305 | EP 2006-771445 | 20060530 |
| | R: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU | | | |
| CN | 101180053 | A | 20080514 | CN 2006-80017617 | 20071121 |
| KR | 2008003933 | A | 20080108 | KR 2007-727922 | 20071129 |
| MX | 200715085 | A | 20080117 | MX 2007-15085 | 20071129 |
| NO | 2007006595 | A | 20071220 | NO 2007-6595 | 20071220 |
| PRAI | US 2005-685848P | P | 20050531 | | |
| | US 2005-692808P | P | 20050622 | | |
| | US 2006-746786P | P | 20060509 | | |
| | WO 2006-US20677 | W | 20060530 | | |

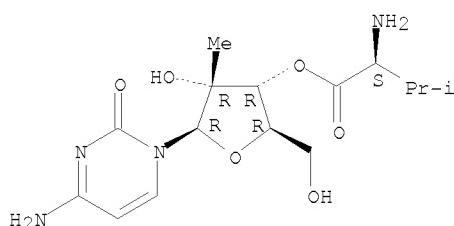
AB The invention discloses use of 4-[3,5-Bis-(2-hydroxyphenyl)-[1,2,4]-triazol-1-yl]benzoic acid for the manufacture of pharmaceutical compns. for the treatment of liver diseases in humans in which iron plays a role in pathogenesis, including viral diseases, e.g. chronic hepatitis C, optionally in conjunction with antiviral agents and for the treatment of nonviral diseases, e.g. non-alc. steatohepatitis and non-alc. fatty liver disease.

IT 640281-90-9, Valopicitabine
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (triazolyl benzoic acid derivative for treatment of liver diseases in which iron plays role in pathogenesis)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

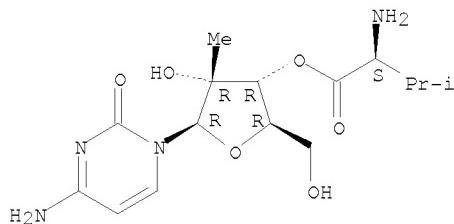


L11 ANSWER 17 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2006:1257296 CAPLUS
 DN 146:54578
 TI Recent patents on nucleoside and nucleotide inhibitors for HCV
 AU Shim, Jae H.; Hong, Zhi; Wu, Jim Z.
 CS Drug Discovery, Valeant Pharmaceuticals International, Costa Mesa, CA, 92626, USA
 SO Recent Patents on Anti-Infective Drug Discovery (2006), 1(3), 323-331
 CODEN: RPADCX; ISSN: 1574-891X
 PB Bentham Science Publishers Ltd.
 DT Journal; General Review
 LA English
 AB A review. Hepatitis C virus (HCV) infection is a leading cause of liver diseases such as cirrhosis and hepatocellular carcinoma. There are estimated 170 million people worldwide chronically infected with the virus. The lack of highly effective and safe therapeutics for HCV infection has spurred intensive efforts to develop anti-HCV drugs as evidenced by the large number of new patent applications filed each year. Nucleoside and nucleotide inhibitors are the analogs of DNA or RNA substrates, and they inhibit viral polymerases by acting as chain terminators, viral mutagens, or simple competitive inhibitors. The successful development of various nucleoside and nucleotide inhibitors for the treatment of HIV and HBV infections has prompted the drug industry to seek similar strategies for HCV. This review summarizes recently issued or published patents covering nucleoside and nucleotide inhibitors for HCV. The claimed chemical structures and available biol. activities, mechanism of action, and drug resistance profiles are discussed. The development status of several promising nucleoside inhibitors is also described.

IT 640725-71-9, NM283
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (recent patents on nucleoside and nucleotide inhibitors for HCV
)

RN 640725-71-9 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

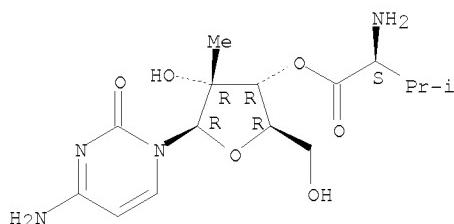


● 2 HCl

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 18 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:1086375 CAPLUS
DN 146:54739
TI Ribavirin antagonizes the in vitro anti-hepatitis C virus activity of 2'-C-methylcytidine, the active component of valopicitabine
AU Coelmont, Lotte; Paeshuyse, Jan; Windisch, Marc P.; De Clercq, Erik; Bartenschlager, Ralf; Neyts, Johan
CS Rega Institute for Medical Research, KULeuven, Louvain, 3000, Belg.
SO Antimicrobial Agents and Chemotherapy (2006), 50(10), 3444-3446
CODEN: AMACQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB Ribavirin antagonizes the in vitro anti-hepatitis C virus (HCV) activity of the pyrimidine nucleoside analog 2'-C-methylcytidine, the active component of the exptl. anti-HCV drug valopicitabine. In contrast, the combination of ribavirin with either the purine nucleoside analog 2'-C-methyladenosine or the HCV protease inhibitor VX-950 resulted in an additive antiviral activity. These findings may have implications when planning clin. studies with valopicitabine.
IT 640281-90-9D, Valopicitabine, metabolite
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ribavirin antagonizes anti-hepatitis C virus activity of 2'-C-methylcytidine, active component of valopicitabine)
RN 640281-90-9 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

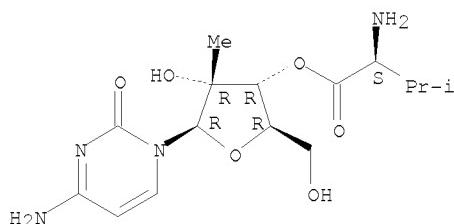


RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 19 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:1045856 CAPLUS
DN 146:28022
TI Synthesis and Pharmacokinetics of Valopicitabine (NM283), an Efficient Prodrug of the Potent Anti-HCV Agent 2'-C-Methylcytidine
AU Pierra, Claire; Amador, Agnes; Benzaria, Samira; Cretton-Scott, Erika; D'Amours, Marc; Mao, John; Mathieu, Steven; Moussa, Adel; Bridges, Edward

G.; Standring, David N.; Sommadossi, Jean-Pierre; Storer, Richard;
Gosselin, Gilles
CS Laboratoire Coopératif Idenix-CNRS-Université Montpellier II Case Courrier
008, Université Montpellier II, Montpellier, 34095, Fr.
SO Journal of Medicinal Chemistry (2006), 49(22), 6614-6620
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 146:28022
AB In the search for new therapeutic agents against chronic hepatitis C, 2'-C-methylcytidine was discovered to be a potent and selective inhibitor in cell culture of a number of RNA viruses, including the pestivirus bovine viral diarrhea virus, a surrogate model for hepatitis C virus (HCV), and three flaviviruses, namely, yellow fever virus, West Nile virus, and dengue-2 virus. However, pharmacokinetic studies revealed that 2'-C-methylcytidine suffers from a low oral bioavailability. To overcome this limitation, the authors have synthesized the 3'-O-L-valinyl ester derivative (NM-283; dihydrochloride salt of valopicitabine) of 2'-C-methylcytidine. The authors present the chemical synthesis and physicochemical characteristics of NM-283, anti-HCV prodrug candidate, as well as a comparative study of its pharmacokinetic parameters with those of its parent nucleoside analog, 2'-C-methylcytidine.
IT 640725-71-9P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and pharmacokinetics of NM-283, a prodrug of anti-HCV agent 2'-C-methylcytidine)
RN 640725-71-9 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

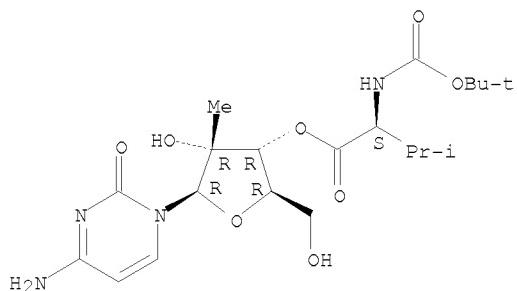
Absolute stereochemistry. Rotation (+).



● 2 HCl

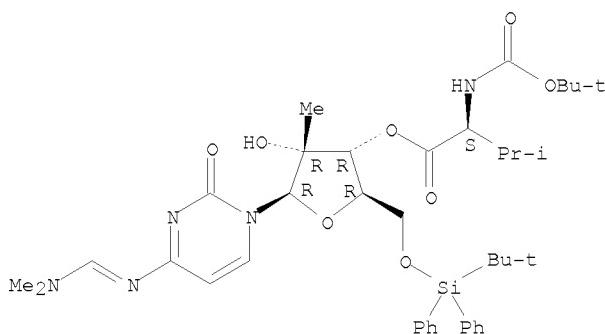
IT 640725-70-8P 642075-44-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and pharmacokinetics of NM-283, a prodrug of anti-HCV
agent 2'-C-methylcytidine)
RN 640725-70-8 CAPLUS
CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with
2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry.



RN 642075-44-3 CAPLUS
 CN L-Valine, N-[1,1-dimethylethoxy carbonyl]-, 3'-ester with
 5'-O-[1,1-dimethyl-ethyl]diphenylsilyl]-N-[(dimethylamino)methylene]-2'-C-
 methylcytidine (CA INDEX NAME)

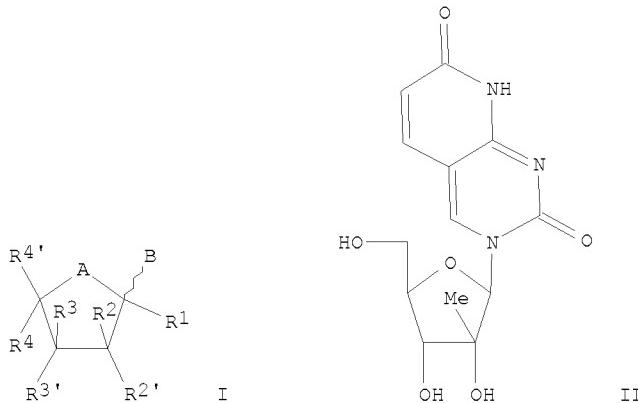
Absolute stereochemistry.
 Double bond geometry unknown.



RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

| | |
|-----------|---|
| L11 | ANSWER 20 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN |
| AN | 2006:945608 CAPLUS |
| DN | 145:315225 |
| TI | Bicyclic nucleosides and nucleotides as therapeutic agents |
| IN | Francom, Paula; Nearn, Roland Henry; Draffan, Alistair George; Lambert, John Nicholas; Bond, Silas |
| PA | Biota, Inc., USA |
| SO | PCT Int. Appl., 107pp. |
| | CODEN: PIXXD2 |
| DT | Patent |
| LA | English |
| FAN.CNT 1 | |
| | PATENT NO. KIND DATE APPLICATION NO. DATE |
| PI | WO 2006094347 A1 20060914 WO 2006-AU303 20060308 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW |
| | RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM |
| | AU 2006222563 A1 20060914 AU 2006-222563 20060308 |
| | CA 2600886 A1 20060914 CA 2006-2600886 20060308 |
| | EP 1858889 A1 20071128 EP 2006-704976 20060308 |

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR
 PRAI US 2005-661665P P 20050308
 WO 2006-AU303 W 20060308
 OS CASREACT 145:315225
 GI

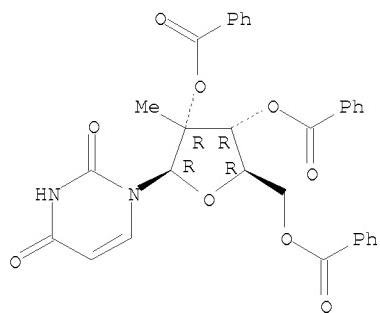


AB The invention relates to the use of bicyclic nucleosides and nucleotides I, wherein: A is O, S, CH₂, CF₂ or NR; B is bicyclic heterocycle; R1, R2, R2', R3, R3', and R4 are independently H, halogen, OH, N₃, CN, alkyl, alkenyl, alkynyl, aryl, acyl, arylalkyl, heterocyclyl, heteroaryl, cycloalkyl, cycloalkenyl, alkyloxy, alkenyloxy, alkynoxy, aryloxy, acyloxy, oxyacyl, arylalkoxy, heterocycloxy, heteroaryloxy, cycloalkoxy, cycloalkenoxy, amino, aminoacyl, aminoacyloxy, acylamino, oxyacylamino, oxyacyloxy, acylimino, acyliminoxy, oxyacylimino, aminothioacyl, thioacylamino, aminosulfinyl, aminosulfonyl, thio, thioacyl, thioacyloxy, oxythioacyl, oxythioacyloxy, optionally; R2 and R2' together or R3 and R3' together represents =O, =S, or =L-Y' where L is N, CH, CF, CCl or CBr and Y' is H, halogen, N₃, Me, Et or CN; R4' is -CY2SH, -CY2OH, -CY2NH, or L'-R5; L' is selected from the group consisting of -CY2-, -CY2CY2-, -CY2OCY2-, -CY2SCY2- and -CY2NHCY2-; Y is H, OR, halogen, alkyl, alkenyl, alkynyl; R5 is OR, NR₂, monophosphate, diphosphate, and triphosphate, or a mono, di or triphosphate mimic; each R is independently H, CF₃, alkyl, alkenyl, alkynyl, aryl, acyl, cycloalkyl, cycloalkenyl, heteroaryl, heterocyclyl; were prepared for the treatment of infectious diseases, and in particular, viral infections. Title compds. were typically active in the replicon assay in the range 1 to >1000 μM and cytotoxic in the range 30 to >100 μM. HCV-polymerase inhibition by title compds. is also reported.

IT 23643-36-9P 909394-67-8P 909394-72-5P
 909394-73-6P 909394-74-7P 909394-75-8P
 909394-76-9P 909394-77-0P 909394-81-6P
 909394-82-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of bicyclic nucleosides and nucleotides as therapeutic agents)

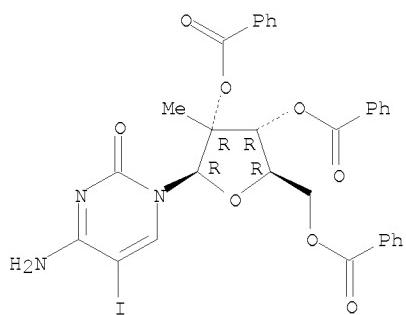
RN 23643-36-9 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2,3,5-tri-O-benzoyl-2-C-methyl-β-D-ribofuranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



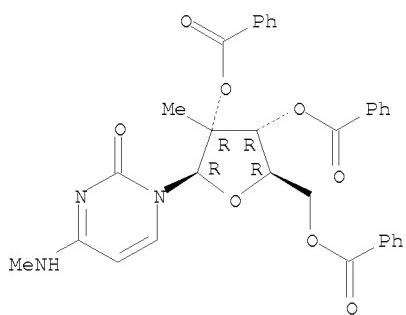
RN 909394-67-8 CAPLUS
CN Cytidine, 5-iodo-2'-C-methyl-, 2',3',5'-tribenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



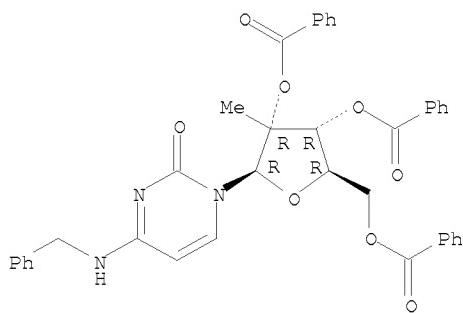
RN 909394-72-5 CAPLUS
CN Cytidine, N-methyl-2'-C-methyl-, 2',3',5'-tribenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



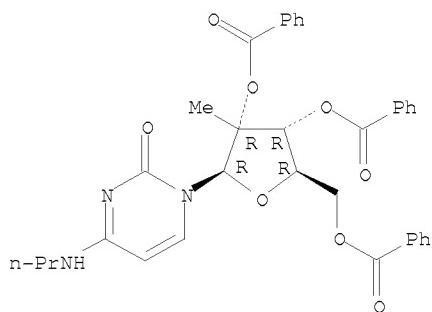
RN 909394-73-6 CAPLUS
CN Cytidine, 2'-C-methyl-N-(phenylmethyl)-, 2',3',5'-tribenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



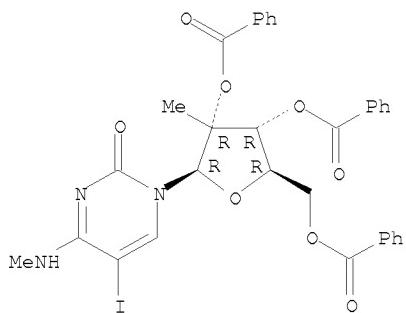
RN 909394-74-7 CAPLUS
 CN Cytidine, 2'-C-methyl-N-propyl-, 2',3',5'-tribenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



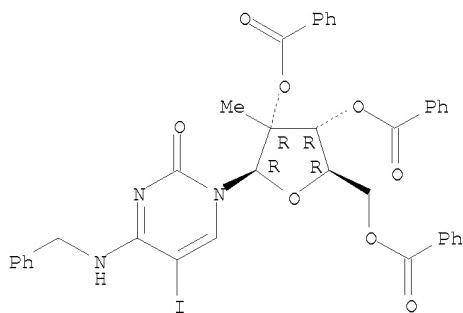
RN 909394-75-8 CAPLUS
 CN Cytidine, 5-iodo-N-methyl-2'-C-methyl-, 2',3',5'-tribenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



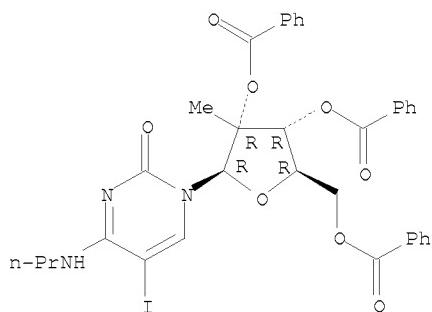
RN 909394-76-9 CAPLUS
 CN Cytidine, 5-iodo-2'-C-methyl-N-(phenylmethyl)-, 2',3',5'-tribenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



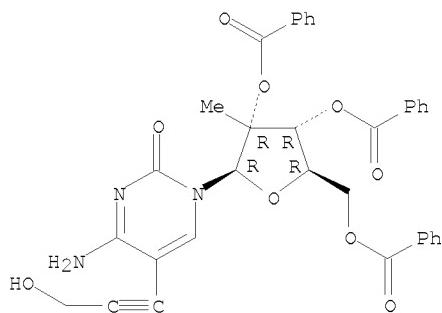
RN 909394-77-0 CAPLUS
 CN Cytidine, 5-iodo-2'-C-methyl-N-propyl-, 2',3',5'-tribenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



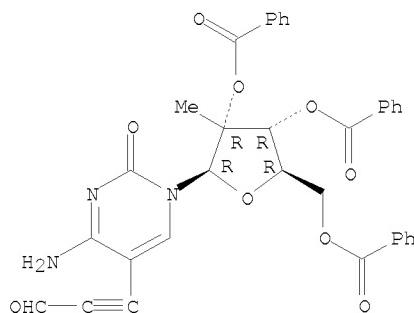
RN 909394-81-6 CAPLUS
 CN Cytidine, 5-(3-hydroxy-1-propynyl)-2'-C-methyl-, 2',3',5'-tribenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 909394-82-7 CAPLUS
 CN Cytidine, 2'-C-methyl-5-(3-oxo-1-propynyl)-, 2',3',5'-tribenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



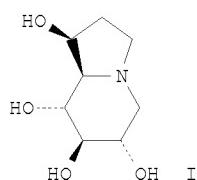
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 21 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:894484 CAPLUS
DN 145:285094
TI Glucosidase inhibitor combinations with adjunctive therapies for treating or preventing Flaviviridae infections
IN Dugourd, Dominique; Rubinchik, Evelina; Clement, Jacob; Friedland, Hillel David
PA Migenix Inc., Can.
SO U.S. Pat. Appl. Publ., 69pp.
CODEN: USXXCO
DT Patent
LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-----------------|--|----------|-----------------|----------|
| PI | US 20060194835 | A1 | 20060831 | US 2006-351885 | 20060209 |
| | AU 2006221080 | A1 | 20060914 | AU 2006-221080 | 20060209 |
| | CA 2597213 | A1 | 20060914 | CA 2006-2597213 | 20060209 |
| | WO 2006096285 | A2 | 20060914 | WO 2006-US4927 | 20060209 |
| | WO 2006096285 | A3 | 20070125 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| | RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| | EP 1853317 | A2 | 20071114 | EP 2006-748202 | 20060209 |
| | R: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | |
| | MX 200709561 | A | 20080114 | MX 2007-9561 | 20070808 |
| | IN 2007KN03225 | A | 20080321 | IN 2007-KN3225 | 20070831 |
| | KR 2007102741 | A | 20071019 | KR 2007-720540 | 20070907 |
| PRAI | US 2005-651910P | P | 20050209 | | |
| | US 2005-664297P | P | 20050321 | | |
| | US 2005-735464P | P | 20051112 | | |
| | WO 2006-US4927 | W | 20060209 | | |

GI



AB The present disclosure relates generally to compns. having a glucosidase inhibitor [castanospermine (I) or a derivative thereof, such as celgosivir] in combination with adjunctive therapies of compds. that alter immune function (such as interferon) and compds. that alter viral replication (such as nucleoside analogs like ribavirin), which can be used to treat or prevent infections caused by or associated with a virus of the Flaviviridae family, particularly infections caused by or associated with Hepatitis C virus (HCV). Examples include synergy of castanospermine or celgosivir in combination with other drugs such as interferons in a checkboard approach.

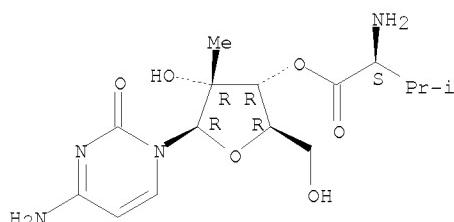
IT 640725-71-9, NM283

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glucosidase inhibitor combinations with adjunctive therapies for treating or preventing Flaviviridae infections)

RN 640725-71-9 CAPLUS

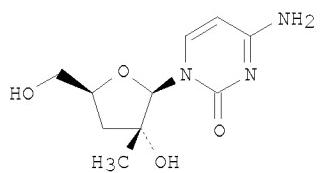
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● 2 HCl

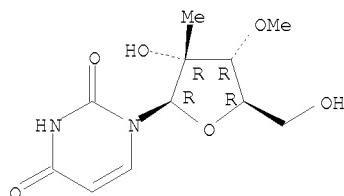
L11 ANSWER 22 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:774481 CAPLUS
DN 146:402230
TI Synthesis of 2'-C-methylcytidine and 2'-C-methyluridine derivatives modified in the 3'-position as potential antiviral agents
AU Pierra, Claire; Amador, Agnes; Badaroux, Eric; Storer, Richard; Gosselin, Gilles
CS Laboratoire Coopératif Idenix-CNRS-Université Montpellier II, Université Montpellier II, Montpellier, 34095/5, Fr.
SO Collection of Czechoslovak Chemical Communications (2006), 71(7), 991-1010
CODEN: CCCCAK; ISSN: 0010-0765
PB Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic
DT Journal
LA English
OS CASREACT 146:402230
GI



AB 2'-C-methylcytidine and 2'-C-methyluridine derivs. modified in the 3'-position, e.g. I·HCl, were prepared via Barton deoxygenation, amination, stereoselective cyclization, ring opening and fluorination from 2'-C-methyluridine or uridine. The antiviral activity of the title compds. was tested against RNA viruses and was found to be inactive. It was found that the modification at the 3'-position resulted in loss of

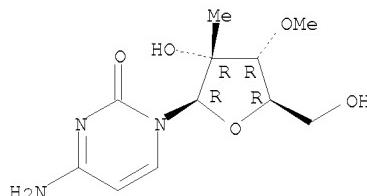
antiviral activity.
 IT 934014-31-0P
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
 (no activity; preparation and antiviral activity of methylcytidine and methyluridine derivs. via Barton deoxygenation, amination, stereoselective cyclization, ring opening and fluorination from methyluridine or uridine)
 RN 934014-31-0 CAPLUS
 CN Uridine, 2'-C-methyl-3'-O-methyl- (CA INDEX NAME)

Absolute stereochemistry.



IT 934014-32-1P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (no activity; preparation and antiviral activity of methylcytidine and methyluridine derivs. via Barton deoxygenation, amination, stereoselective cyclization, ring opening and fluorination from methyluridine or uridine)
 RN 934014-32-1 CAPLUS
 CN Cytidine, 2'-C-methyl-3'-O-methyl-, hydrochloride (1:1) (CA INDEX NAME)

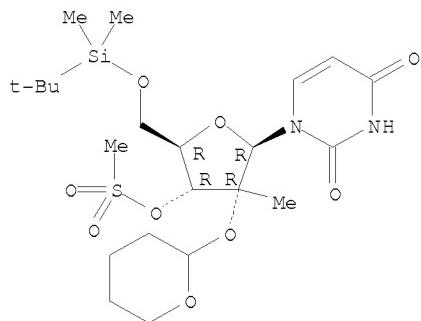
Absolute stereochemistry.



● HCl

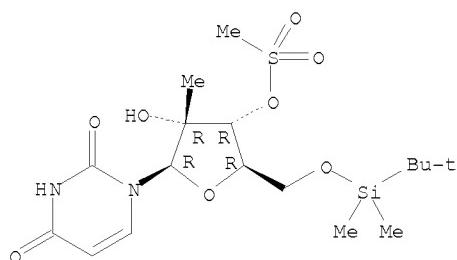
IT 934014-23-0P 934014-24-1P 934014-27-4P
 934014-28-5P 934014-30-9P 934014-42-3P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and antiviral activity of methylcytidine and methyluridine derivs. via Barton deoxygenation, amination, stereoselective cyclization, ring opening and fluorination from methyluridine or uridine)
 RN 934014-23-0 CAPLUS
 CN Uridine, 5'-O-[(1,1-dimethylethyl)dimethylsilyl]-2'-C-methyl-2'-O-(tetrahydro-2H-pyran-2-yl)-, 3'-methanesulfonate (CA INDEX NAME)

Absolute stereochemistry.



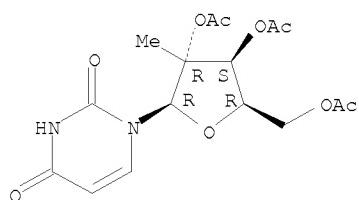
RN 934014-24-1 CAPLUS
CN Uridine, 5'-O-[1,1-dimethylethyl]dimethylsilyl]-2'-C-methyl-,
3'-methanesulfonate (CA INDEX NAME)

Absolute stereochemistry.



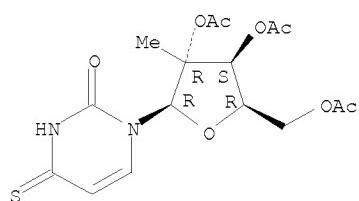
RN 934014-27-4 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2,3,5-tri-O-acetyl-2-C-methyl-beta-D-xylofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry.



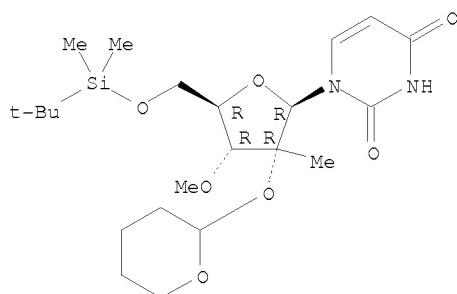
RN 934014-28-5 CAPLUS
CN 2(1H)-Pyrimidinone, 3,4-dihydro-4-thioxo-1-(2,3,5-tri-O-acetyl-2-C-methyl-beta-D-xylofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry.



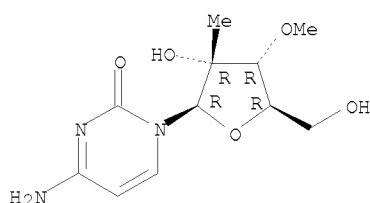
RN 934014-30-9 CAPLUS
CN Uridine, 5'-O-[1,1-dimethylethyl]dimethylsilyl]-2'-C-methyl-3'-O-methyl-,
2'-O-(tetrahydro-2H-pyran-2-yl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 934014-42-3 CAPLUS
 CN Cytidine, 2'-C-methyl-3'-O-methyl- (CA INDEX NAME)

Absolute stereochemistry.



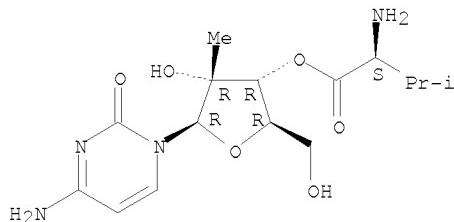
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L11 ANSWER 23 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2006:708636 CAPLUS
 DN 146:19039
 TI Valopicitabine: anti-hepatitis C virus drug
 RNA-directed RNA polymerase (NS5B) inhibitor
 AU Sorbera, L. A.; Castaner, J.; Leeson, P. A.
 CS Prous Science, Barcelona, 08080, Spain
 SO Drugs of the Future (2006), 31(4), 320-324
 CODEN: DRFUD4; ISSN: 0377-8282
 PB Prous Science
 DT Journal; General Review
 LA English
 AB A review. Chronic hepatitis C is caused by infection with the hepatitis C virus (HCV), a member of the Flaviviridae family of viruses. Currently available treatment for HCV, including the standard combination therapy with interferon and ribavirin, is often unsuccessful at eradicating infection. In addition, the therapies now used to treat chronic hepatitis C are associated with substantial side effects. Therefore, new therapeutic strategies such as the use of antiviral drugs targeted to HCV-specific viral enzymes are being explored. One such option is the RNA-directed RNA polymerase (NS5B) inhibitor valopicitabine (NM-283), an orally bioavailable prodrug of the novel ribonucleoside analog NM-107. This compound has shown in vitro activity against HCV-related bovine viral diarrhea virus (BVDV) polymerase. In patients with HCV-1 infection, valopicitabine produced reductions in HCV RNA viral load when administered either as monotherapy or in combination with pegylated interferon. When used together, valopicitabine and interferon appear to have synergistic antiviral effects both in vitro and in vivo. The compound is generally well tolerated, with gastrointestinal effects being the most commonly observed treatment-related adverse events.
 IT 640725-71-9P, NM-283
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (valopicitabine reduced HCV RNA viral load either as

monotherapy or in combination with pegylated interferon against HCV-related bovine viral diarrhea virus polymerase and in patient with hepatitis C virus-1 infection)

RN 640725-71-9 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

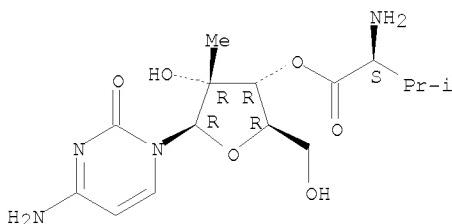


●2 HCl

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L11 ANSWER 24 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2006:425398 CAPLUS
 DN 145:39734
 TI Nucleoside analog inhibitors of hepatitis C virus replication
 AU Carroll, S. S.; Olsen, D. B.
 CS Department of Antiviral Research, Merck Research Laboratories, West Point, PA, 19486, USA
 SO Infectious Disorders: Drug Targets (2006), 6(1), 17-29
 CODEN: IDDTAD; ISSN: 1871-5265
 PB Bentham Science Publishers Ltd.
 DT Journal; General Review
 LA English
 AB A review. Of the 30 compds. currently marketed in the United States for treatment of viral infections, 15 are nucleoside analogs, demonstrating the utility of this class of compound as a source of antiviral drugs. The success of nucleoside analogs in treating other viral infections provides a compelling rationale for the significant effort that is currently being devoted to the discovery and development of nucleoside analogs to treat infection by hepatitis C virus (HCV) that may lead to improvements in response rates compared to currently available therapies. Several different approaches were adopted to identify promising analogs, including the use of surrogate viruses in cell culture assays, screening in the cell-based bicistronic HCV replicon assay, and screening nucleoside triphosphates for the ability to inhibit the activity of the HCV RNA-dependent RNA polymerase in vitro. Several classes of ribonucleoside analogs with modifications of the ribose inhibit HCV replication. Nucleoside analogs incorporating a 2'-C-Me modification are potent inhibitors in the replicon assay in the absence of cytotoxicity, and appear to exert their inhibition by acting as functional chain terminators of RNA synthesis. NM283, a prodrug of 2'-C-methylcytidine, has entered clin. trials and demonstrated viral load redns. in subjects infected with genotype 1 HCV, a genotype known to be difficult to treat effectively with currently approved therapies. Overall, results to date offer encouragement that improved therapies to treat HCV infection including newly developed nucleoside analogs may become available within the next few years.
 IT 640725-71-9, NM 283
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (nucleoside analog inhibitors of hepatitis C virus replication)
 RN 640725-71-9 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● 2 HCl

RE.CNT 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 25 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2006:342840 CAPLUS
 DN 144:381956
 TI Combination antiviral compositions comprising castanospermine and use for the treatment and prevention of infections caused by or associated with a virus of the Flaviviridae family
 IN Dugourd, Dominique
 PA Migenix Inc., Can.
 SO PCT Int. Appl., 54 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|----------|
| PI WO 2006037227 | A1 | 20060413 | WO 2005-CA1528 | 20051006 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ,
NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,
SK, SI, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN,
YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
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KG, KZ, MD, RU, TJ, TM | | | | |
| AU 2005291804 | A1 | 20060413 | AU 2005-291804 | 20051006 |
| CA 2583351 | A1 | 20060413 | CA 2005-2583351 | 20051006 |
| US 20060093577 | A1 | 20060504 | US 2005-244811 | 20051006 |
| EP 1802327 | A1 | 20070704 | EP 2005-794475 | 20051006 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | | |
| CN 101035555 | A | 20070912 | CN 2005-80034258 | 20051006 |
| JP 2008515816 | T | 20080515 | JP 2007-534981 | 20051006 |
| MX 200703853 | A | 20071121 | MX 2007-3853 | 20070329 |
| KR 2007061879 | A | 20070614 | KR 2007-708715 | 20070417 |
| IN 2007KN01353 | A | 20070720 | IN 2007-KN1353 | 20070417 |
| PRAI US 2004-616787P | P | 20041006 | | |
| WO 2005-CA1528 | W | 20051006 | | |
| AB The invention discloses the use of castanospermine in combination with another therapeutic agent to treat or prevent infections caused by or associated with a virus of the Flaviviridae family, particularly infections caused by or associated with Hepatitis C virus (HCV), and to the use of such compds. to examine the biol. mechanisms of HCV infection. | | | | |
| IT 882489-96-5 | | | | |
| RL: BSU (Biological study, unclassified); BIOL (Biological study)
(castanospermine-containing combination antiviral compns., and use for treatment of Flaviviridae infections) | | | | |

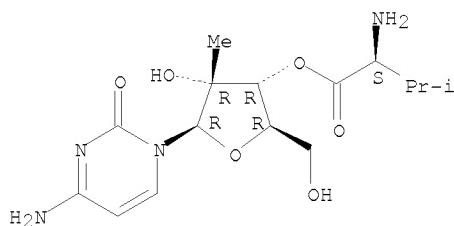
10/609,298

RN 882489-96-5 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, mixt. with
(1S,6S,7R,8R,8aR)-octahydro-1,6,7,8-indolizinetetrol (9CI) (CA INDEX
NAME)

CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

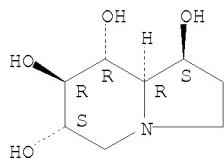
Absolute stereochemistry. Rotation (+).



CM 2

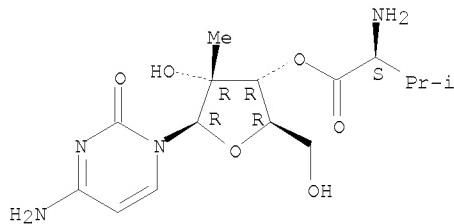
CRN 79831-76-8
CMF C8 H15 N O4

Absolute stereochemistry. Rotation (+).



IT 640281-90-9, Valopicitabine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(castanospermine-containing combination antiviral compns., and use for
treatment of Flaviviridae infections)
RN 640281-90-9 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 26 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:149315 CAPLUS
DN 144:205728
TI Methods using a Type II interferon receptor agonist alone or in
combination with a direct antiviral drug for treating hepatitis
C virus infection
IN Blatt, Lawrence M.

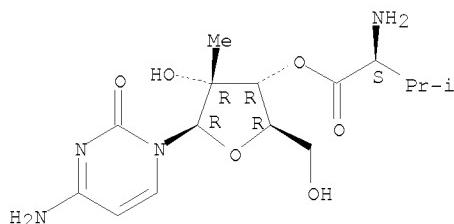
McIntosh

PA Intermune, Inc., USA
 SO PCT Int. Appl., 139 pp.
 CODEN: PIXXD2

DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--|--|----------|-----------------|----------|
| PI | WO 2006016930 | A2 | 20060216 | WO 2005-US16927 | 20050513 |
| | WO 2006016930 | A3 | 20060803 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
ZA, ZM, ZW | | | |
| | RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM,
KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG,
KZ, MD, RU, TJ, TM | | | |
| PRAI | US 2004-571322P | P | 20040514 | | |
| AB | The invention provides methods for treating hepatitis C virus (HCV) infection; methods for reducing the incidence of complications associated with HCV and cirrhosis of the liver; and methods for reducing viral load, or reducing the time to viral clearance, or reducing morbidity or mortality in the clin. outcomes, in patients suffering from HCV infection. The methods generally involve administering to the individual a Type II interferon receptor agonist alone or in combination with a direct antiviral drug. | | | | |
| IT | 640725-71-9, NM 283
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type II interferon receptor agonist alone or in combination with direct antiviral drug for treating hepatitis C virus infection) | | | | |
| RN | 640725-71-9 CAPLUS | | | | |
| CN | L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME) | | | | |

Absolute stereochemistry. Rotation (+).



● 2 HCl

L11 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2006:103884 CAPLUS
 DN 144:171198
 TI Preparation of alkyl-substituted 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs via condensation of the lactone to nucleosides as potential antiviral agents
 IN Wang, Peiyuan; Stec, Wojciech; Clark, Jeremy; Chun, Byoung-Kwon; Shi, Junxing; Du, Jinfa
 PA Pharmasset, Inc., USA
 SO PCT Int. Appl., 34 pp.
 CODEN: PIXXD2
 DT Patent
 LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|------------------|----------|
| PI | WO 2006012440 | A2 | 20060202 | WO 2005-US25916 | 20050721 |
| | WO 2006012440 | A3 | 20060727 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| AU | 2005267051 | A1 | 20060202 | AU 2005-267051 | 20050721 |
| CA | 2574651 | A1 | 20060202 | CA 2005-2574651 | 20050721 |
| EP | 1773856 | A2 | 20070418 | EP 2005-775359 | 20050721 |
| | R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | | |
| CN | 101023094 | A | 20070822 | CN 2005-80031530 | 20050721 |
| BR | 2005012104 | A | 20080311 | BR 2005-12104 | 20050721 |
| JP | 2008507547 | T | 20080313 | JP 2007-522763 | 20050721 |
| US | 20060199783 | A1 | 20060907 | US 2006-353597 | 20060213 |
| MX | 200700803 | A | 20070402 | MX 2007-803 | 20070119 |
| IN | 2007KN00605 | A | 20070706 | IN 2007-KN605 | 20070220 |
| KR | 2007114344 | A | 20071203 | KR 2007-703980 | 20070220 |
| PRAI | US 2004-589866P | P | 20040721 | | |
| | US 2004-608320P | P | 20040909 | | |
| | US 2005-185988 | A1 | 20050721 | | |
| | WO 2005-US25916 | W | 20050721 | | |
| OS | MARPAT 144:171198 | | | | |
| GI | | | | | |

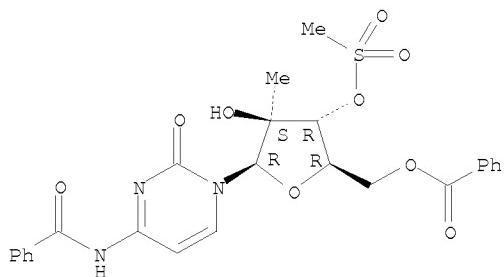
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A process for preparing of 2-deoxy-2-fluoro-2-methyl-D-ribonolactones, I, wherein R1 and R2 can independently be H, CH₃, acetyl, benzoyl, pivaloyl, 4-nitrobenzoyl, 3-nitrobenzoyl, 2-nitrobenzoyl, 4-chlorobenzoyl, 3-chlorobenzoyl, 2-chlorobenzoyl, 4-methylbenzoyl, 3-methylbenzoyl, 2-methylbenzoyl, 4-phenylbenzoyl, benzyl, 4-methoxybenzyl, trityl, trialkylsilyl, t-butyl-dialkylsilyl, t-butylidiphenylsilyl, TIPDS, THP, MOM, or MEM are prepared and used in the condensation to 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs. Thus, 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs II and III, wherein X is a halogen; Y is N or CH; Z is a halogen, hydroxyl, ether, thiol, thioether, (un)substituted amine or alkyl; R1' is alkyl, vinyl, ethynyl; R2' and R3' can be same or different H, alkyl, arylalkyl, acyl, cyclic acetal such as 2',3'-O-isopropylidene or 2',3-O-benzylidene, or 2',3'-cyclic carbonate; R4, R5, and R6 are independently H, halogen, hydroxyl, ether, thiol, thioether, N₃, (un)substituted amine, (un)substituted amido, alkyl, halogenated alkyl, alkenyl, halogenated alkenyl, alkynyl, halogenated alkynyl, hydroxy alkyl, alkoxy are prepared and are potential anti-HCV agents. Specifically, IV was prepared (no yield, claimed) via condensation, alkylation and stereoselective fluorination reactions and can exhibit potential use as an anti-HCV agent.

IT 874638-81-0P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of alkyl-substituted 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs via condensation of the lactone to nucleosides)

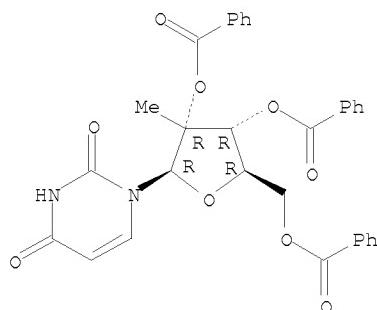
RN 874638-81-0 CAPLUS
CN Benzamide, N-[1-[5-O-benzoyl-2-C-methyl-3-O-(methylsulfonyl)-β-D-arabinofuranosyl]-1,2-dihydro-2-oxo-4-pyrimidinyl]-(CA INDEX NAME)

Absolute stereochemistry.



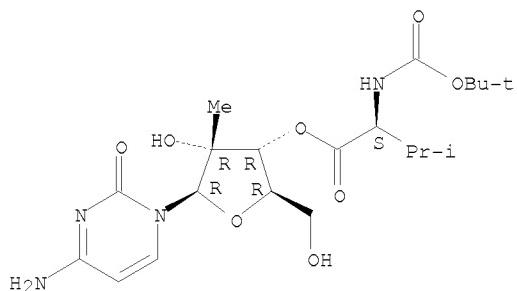
L11 ANSWER 28 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2005:1151389 CAPLUS
 DN 145:271979
 TI NM 283, an efficient prodrug of the potent anti-HCV agent
 2'-C-methylcytidine
 AU Pierra, C.; Benzaria, S.; Amador, A.; Moussa, A.; Mathieu, S.; Storer, R.;
 Gosselin, G.
 CS Laboratoire Cooperatif Idenix, CNRS, Universite Montpellier II,
 Montpellier, 34296, Fr.
 SO Nucleosides, Nucleotides & Nucleic Acids (2005), 24(5-7), 767-770
 CODEN: NNNAFY; ISSN: 1525-7770
 PB Taylor & Francis, Inc.
 DT Journal
 LA English
 OS CASREACT 145:271979
 AB In order to improve the oral bioavailability of 2'-C-methylcytidine, a
 potent anti-HCV agent, the corresponding 3'-O-L-valinyl ester
 derivative (NM 283) has been synthesized. Based on its ease of synthesis and
 its physicochem. properties, NM 283 has emerged as a promising antiviral
 drug for treatment of chronic HCV infection.
 IT 23643-36-9P 640725-70-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation of NM 283 as efficient prodrug of potent anti-HCV
 agent 2'-C-methylcytidine)
 RN 23643-36-9 CAPLUS
 CN 2,4(1H,3H)-Pyrimidinedione, 1-(2,3,5-tri-O-benzoyl-2-C-methyl-β-D-
 ribofuranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



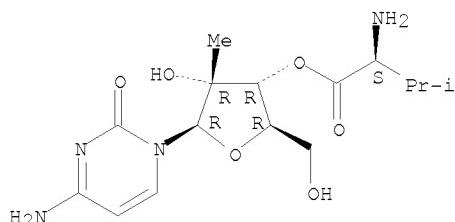
RN 640725-70-8 CAPLUS
 CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with
 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry.



IT 640725-71-9P
 RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prodrug; preparation of NM 283 as efficient prodrug of potent anti-
 HCV agent 2'-C-methylcytidine)
 RN 640725-71-9 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA
 INDEX NAME)

Absolute stereochemistry. Rotation (+).



● 2 HCl

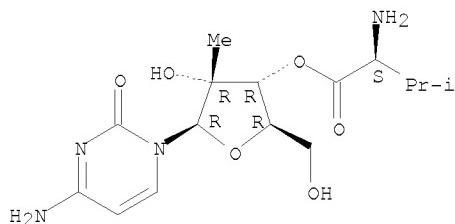
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 29 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2005:684531 CAPLUS
 DN 143:431740
 TI Emerging drugs for chronic hepatitis C
 AU Bhopale, Girish Mahadeorao; Nanda, Rabindra Kumar
 CS Research and Development Division, Hindustan Antibiotics Limited, Pimpri,
 Pune, 411018, India
 SO Hepatology Research (2005), 32(3), 146-153
 CODEN: HPRSFH; ISSN: 1386-6346
 PB Elsevier B.V.
 DT Journal; General Review
 LA English
 AB A review. Hepatitis C virus (HCV) is a major cause of chronic hepatitis, liver cirrhosis and hepatocellular carcinoma worldwide. A combination therapy comprising pegylated interferon and ribavirin currently represents the most effective therapy for chronic HCV infection. The limitations of this current therapy mainly its efficacy and significant side effects have prompted the development of new drugs. Few categories of therapeutic agents appear promising for future therapy, e.g. novel interferons, ribavirin analogs, antisense oligonucleotides, short interfering RNAs, ribozymes, enzyme inhibitors, immunomodulatory agents, antifibrotic agents, therapeutic vaccines and antibodies. Few drugs belong to afore-mentioned categories have already reached the different clin. phases of development. The present article highlights the status of current available therapies and emerging drugs for the treatment of hepatitis C.
 IT 640725-71-9, NM 283
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
 (NM283 proved promising therapeutic effect in treating chronic hepatitis C patient)

RN 640725-71-9 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

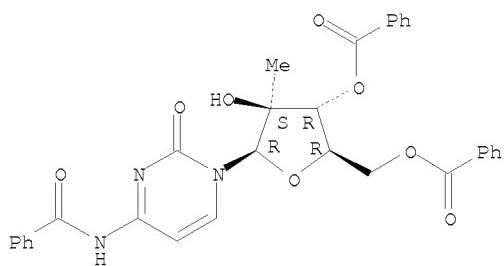


● 2 HCl

RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

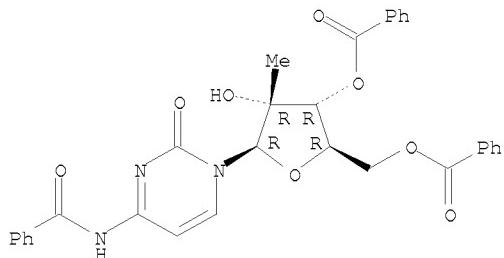
- L11 ANSWER 30 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2005:648160 CAPLUS
 DN 143:248607
 TI Design, Synthesis, and Antiviral Activity of 2'-Deoxy-2'-fluoro-2'-C-methyl-cytidine, a Potent Inhibitor of Hepatitis C Virus Replication
 AU Clark, Jeremy L.; Hollecker, Laurent; Mason, J. Christian; Stuyver, Lieven J.; Tharnish, Phillip M.; Lostia, Stefania; McBrayer, Tamara R.; Schinazi, Raymond F.; Watanabe, Kyoichi A.; Otto, Michael J.; Furman, Phillip A.; Stec, Wojciech J.; Patterson, Steven E.; Pankiewicz, Krzysztof W.
 CS Pharmasset, Inc., Princeton, NJ, 08540, USA
 SO Journal of Medicinal Chemistry (2005), 48(17), 5504-5508
 CODEN: JMCMAR; ISSN: 0022-2623
 PB American Chemical Society
 DT Journal
 LA English
 OS CASREACT 143:248607
 AB The pyrimidine nucleoside- β-D-2'-deoxy-2'-fluoro-2'-C-methylcytidine (I) was designed as a hepatitis C virus RNA-dependent RNA polymerase (HCV RdRp) inhibitor. The title compound was obtained by a DAST fluorination of N4-benzoyl-1-(2-methyl-3,5-di-O-benzoyl-β-D-arabinofuranosyl)cytosine to provide N4-benzoyl-1-(2-fluoro-2-methyl-3,5-di-O-benzoyl-β-D-ribofuranosyl)cytosine. The protected 2'-C-methylcytidine was obtained as a byproduct from the DAST fluorination and allowed for the preparation of two biol. active compds. from a common precursor. Compound I and 2'-C-methylcytidine were assayed in a sub-genomic HCV replicon assay system and found to be potent and selective inhibitors of HCV replication. Compd.I shows increased inhibitory activity in the HCV replicon assay compared to 2'-C-methylcytidine and low cellular toxicity.
 IT 863329-62-8P 863329-64-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (design, synthesis via fluorination, and antiviral activity of 2'-deoxy-2'-fluoro-2'-C-methyl-cytidine, a potent inhibitor of Hepatitis C virus replication)
 RN 863329-62-8 CAPLUS
 CN Benzamide, N-[1-(3,5-di-O-benzoyl-2-C-methyl-β-D-arabinofuranosyl)-1,2-dihydro-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 863329-64-0 CAPLUS
 CN Cytidine, N-benzoyl-2'-C-methyl-, 3',5'-dibenzoate (9CI) (CA INDEX NAME)

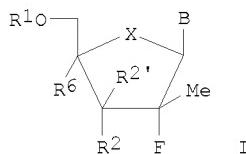
Absolute stereochemistry. Rotation (+).



RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

| L11 | ANSWER 31 OF 37 CAPLUS | COPYRIGHT 2008 ACS on STN | | |
|--|---|---------------------------|------------------|----------|
| AN | 2005:34765 | CAPLUS | | |
| DN | 142:94074 | | | |
| TI | Preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleoside analogs as antiviral agents | | | |
| IN | Clark, Jeremy | | | |
| PA | Pharmasset, Ltd., Barbados | | | |
| SO | PCT Int. Appl., 228 pp. | | | |
| | CODEN: PIXXD2 | | | |
| DT | Patent | | | |
| LA | English | | | |
| FAN.CNT 1 | | | | |
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
| ----- | ----- | ----- | ----- | ----- |
| PI WO 2005003147 | A2 | 20050113 | WO 2004-US12472 | 20040421 |
| WO 2005003147 | A3 | 20050303 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
TD, TG | | | | |
| AU 2004253860 | A2 | 20050113 | AU 2004-253860 | 20040421 |
| AU 2004253860 | A1 | 20050113 | | |
| CA 2527657 | A1 | 20050113 | CA 2004-2527657 | 20040421 |
| US 20050009737 | A1 | 20050113 | US 2004-828753 | 20040421 |
| EP 1633766 | A2 | 20060315 | EP 2004-775900 | 20040421 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| BR 2004010846 | A | 20060627 | BR 2004-10846 | 20040421 |
| CN 1816558 | A | 20060809 | CN 2004-80019148 | 20040421 |
| JP 2006526629 | T | 20061124 | JP 2006-513231 | 20040421 |
| MX 2005PA12788 | A | 20060222 | MX 2005-PA12788 | 20051125 |
| IN 2005DN06087 | A | 20080509 | IN 2005-DN6087 | 20051227 |

| | | | |
|----------------------|-------------|----------------|----------|
| NO 2005006221 | A 20051228 | NO 2005-6221 | 20051228 |
| US 20080070861 | A1 20080320 | US 2007-854218 | 20070912 |
| PRAI US 2003-474368P | P 20030530 | | |
| US 2004-828753 | A3 20040421 | | |
| WO 2004-US12472 | W 20040421 | | |
| OS MARPAT 142:94074 | | | |
| GI | | | |

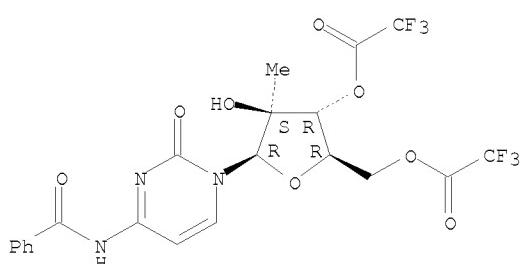


AB The disclosed invention provides nucleoside analogs I, wherein B is purine and pyrimidine nucleobase; X is O, S, CH₂, Se, NH, N-alkyl, CHW, C(W)2; W is F, Cl, Br, iodo; R1 is H, phosphate, H-phosphonate, acyl, Ph, alkyl, carboxyalkylamino, sulfonate ester, peptide, amino acid, sugar residue; R2 and R2' are independently H, alkyl, alkenyl, alkynyl, vinyl, N3, CN, halogen, NO₂, ester, alkoxy, thioalkyl, sulfoxide, sulfonyl; R6 is alkyl, CN, Me, OMe, OEt, CH₂OH, CH₂F, N3, CHCN, CH₂N₃, CH₂NH₂, CH₂NHMe, CH₂NMe₂, alkynylne; and methods of treating a Flaviviridae infection, including hepatitis C virus, West Nile Virus, yellow fever virus, and a rhinovirus infection in a host, including animals, and especially human, using a (2'R)-2'-deoxy-2'-fluoro-2'-C-Me nucleosides, or a pharmaceutically acceptable salt or prodrug thereof. Thus, (2'R)-2'-deoxy-2'-fluoro-2'-C-methylcytidine was prepared and tested as antiviral agent. The effects the nucleoside analogs tested on human bone marrow cells are reported. (2'R)-2'-deoxy-2'-fluoro-2'-C-methylcytidine shows activity against Rhinovirus, West Nile virus, Yellow Fever virus, and Dengue virus. Cytotoxicity and effect of nucleoside analogs on human bone marrow cells are reported.

IT 817204-36-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-Me nucleoside analogs as antiviral agents)

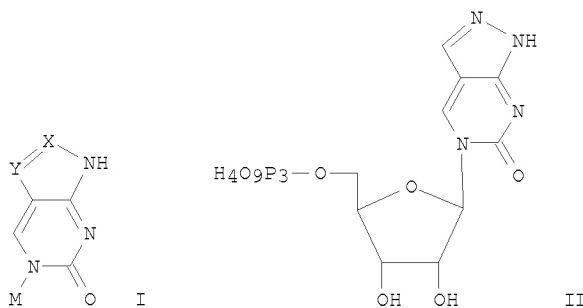
RN 817204-36-7 CAPLUS
CN Benzamide, N-[1,2-dihydro-1-[2-C-methyl-3,5-bis-O-(trifluoroacetyl)-β-D-arabinofuranosyl]-2-oxo-4-pyrimidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 32 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:780543 CAPLUS
DN 141:296247
TI Preparation of cytidine nucleoside analogs as antiviral agents
IN Girardet, Jean-Luc; Koh, Yung-Hyo; An, Haoyun; Hong, Zhi
PA Ribapharm Inc., USA
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

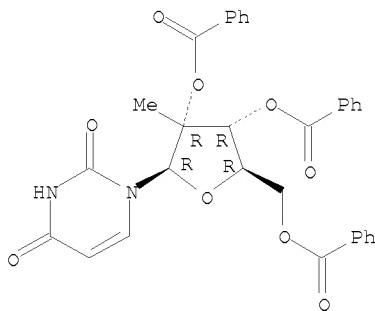
| PATENT NO. | | KIND | DATE | APPLICATION NO. | | DATE |
|------------|--|------|----------|-----------------|--|----------|
| PI | WO 2004080466 | A1 | 20040923 | WO 2003-US6992 | | 20030307 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
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BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | | |
| | AU 2003225705 | A1 | 20040930 | AU 2003-225705 | | 20030307 |
| PRAI | WO 2003-US6992 | A | 20030307 | | | |
| OS | MARPAT 141:296247 | | | | | |
| GI | | | | | | |



AB Cytidine analogs I, wherein -X=Y- is -N=N-, -CH=N-, -N=N=CZ- or -CH=CN-, wherein Z is H, halogen, or alkyl, and wherein M is a sugar or sugar analog; wherein the compound has a D-configuration or an L-configuration; with the proviso that where M is a substituted sugar with a ribofuranose ring having a heteroatom and substituents R1 and R2 on the C3'-atom, R3 and R4 on the C2'-atom, and R5 on the C5'-atom, R1-R4 together are not independently H, OH, F, NH₂, N₃, O-hydrocarbyl, or a reporter moiety, when the heteroatom is O, S, Se, SO, N-alkyl, or CH₂, and when R5 is OH, SH, NH₂, monophosphate, diphosphate, triphosphate, thiophosphate, or boranophosphate; and with the further proviso that M does not comprise a cyclopropenyl group, a morpholino group, or M is not a phosphorylmethoxyethyl, their prodrugs and/or metabolites are employed as pharmaceutically active compds. for treatment of diseases responsive to such compds. Particularly preferred diseases include viral diseases (e.g., HCV infection) and neoplasms (no biol. data). Thus nucleoside analog II was prepared and tested as antiviral agent. The virus is an HCV virus, an HIV virus, an RSV virus, an influenza virus, or a HBV virus.

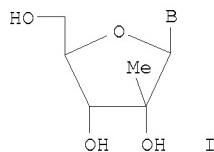
IT 23643-36-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of cytidine nucleoside analogs as antiviral agents)
RN 23643-36-9 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2,3,5-tri-O-benzoyl-2-C-methyl-β-D-
ribofuranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

| L11 | ANSWER 33 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN | | | |
|---|---|----------|------------------|----------|
| AN | 2004:566635 CAPLUS | | | |
| DN | 141:89323 | | | |
| TI | Process for the production of 3'-nucleoside prodrugs | | | |
| IN | Storer, Richard; Moussa, Adel; Mathieu, Steven; Qu, Lin | | | |
| PA | Idenix Cayman Limited, Cayman I. | | | |
| SO | PCT Int. Appl., 57 pp.
CODEN: PIXXD2 | | | |
| DT | Patent | | | |
| LA | English | | | |
| FAN.CNT 1 | | | | |
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
| PI WO 2004058792 | A1 | 20040715 | WO 2003-US41603 | 20031223 |
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CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO,
NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
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| CA 2511616 | A1 | 20040715 | CA 2003-2511616 | 20031223 |
| AU 2003300434 | A1 | 20040722 | AU 2003-300434 | 20031223 |
| US 20040181051 | A1 | 20040916 | US 2003-746395 | 20031223 |
| EP 1575971 | A1 | 20050921 | EP 2003-814400 | 20031223 |
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IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003016868 | A | 20051025 | BR 2003-16868 | 20031223 |
| CN 1751058 | A | 20060322 | CN 2003-80109820 | 20031223 |
| JP 2006514038 | T | 20060427 | JP 2004-562599 | 20031223 |
| NZ 540913 | A | 20080229 | NZ 2003-540913 | 20031223 |
| ZA 2005005040 | A | 20060426 | ZA 2005-5040 | 20050621 |
| NO 2005003557 | A | 20050908 | NO 2005-3557 | 20050720 |
| PRAI US 2002-436150P | P | 20021223 | | |
| WO 2003-US41603 | W | 20031223 | | |
| OS CASREACT 141:89323; MARPAT 141:89323 | | | | |
| GI | | | | |

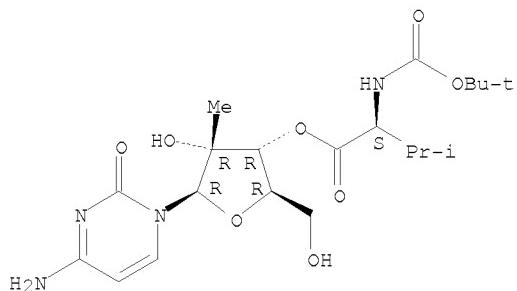


AB Provided is a single-step process for the regioselective 3'-acylation of a ribofuranosyl 2'- or 3'-branched nucleosides I, wherein B is nucleobase.

These compds. are useful as antiviral agents, and in particular, can be used to treat Flaviviridae infections in a host in need thereof (no data). Thus, 9-(2'-C-methyl-3'-O-valinoyl- β -D-ribofuranosyl)-6-N-methyladenine dihydrochloride was prepared via regioselective esterification of 9-(2'-C-methyl- β -D-ribofuranosyl)-6-N-methyladenine with N-(tert-butoxycarbonyl)-L-valine.

IT 640725-70-8P
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
 (process for production of nucleoside prodrugs via regioselective esterification)
 RN 640725-70-8 CAPLUS
 CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry.

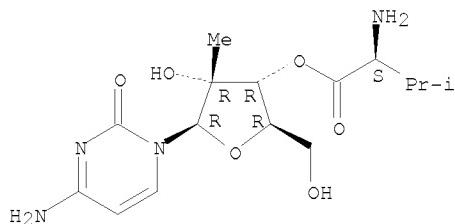


L11 ANSWER 34 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2004:453348 CAPLUS
 DN 141:17578
 TI Treatment of Flaviviridae infection with 2'-branched nucleosides and another mutation-inducing drug such as interferon
 IN Sommadossi, Jean-Pierre; La Colla, Paolo; Standring, David; Bichko, Vadim; Qu, Lin
 PA Idenix (Cayman) Limited, Cayman I.; Universita Degli Studi Di Cagliari
 SO PCT Int. Appl., 166 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|----------|
| PI WO 2004046331 | A2 | 20040603 | WO 2003-US36714 | 20031117 |
| WO 2004046331 | A3 | 20060302 | | |
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| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2506129 | A1 | 20040603 | CA 2003-2506129 | 20031117 |
| AU 2003298658 | A1 | 20040615 | AU 2003-298658 | 20031117 |
| US 20050031588 | A1 | 20050210 | US 2003-715729 | 20031117 |
| EP 1576138 | A2 | 20050921 | EP 2003-796412 | 20031117 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003016363 | A | 20051004 | BR 2003-16363 | 20031117 |
| JP 2006519753 | T | 20060831 | JP 2004-553823 | 20031117 |
| CN 1849142 | A | 20061018 | CN 2003-80108747 | 20031117 |
| MX 2005PA05192 | A | 20050908 | MX 2005-PA5192 | 20050513 |
| NO 2005002920 | A | 20050815 | NO 2005-2920 | 20050615 |
| PRAI US 2002-426675P | P | 20021115 | | |
| WO 2003-US36714 | W | 20031117 | | |

OS MARPAT 141:17578
 AB The present invention discloses a method for the treatment of Flaviviridae infection that includes the administration of a 2'-branched nucleoside, or a pharmaceutically acceptable prodrug and/or salt thereof, to a human in need of therapy in combination or alternation with a drug that directly or indirectly induces a mutation in the viral genome at a location other than a mutation of a nucleotide that results in a change from serine to a different amino acid in the highly conserved consensus sequence, $\text{XRX}^{\text{u}}\text{S}^{\text{x}}\text{GXXXT}$, of domain B of the RNA polymerase region, or is associated with such a mutation. The invention also includes a method to detect a mutant strain of Flaviviridae and a method for its treatment. Thus, in bovine viral diarrhea virus (BVDV)-infected MDBK cells treated with β -D-2'-methylcytidine, viruses resistant to the nucleoside appeared. The drug resistance was associated with a mutation in the NS5B gene which resulted in an S405T substitution in the encoded RNA-dependent RNA polymerase. These mutant viruses were sensitive to Intron A (interferon α -2b). Intron A and β -D-2'-methylcytidine exhibited synergistic inhibitory activity on BVDV growth in MDBK cells.
 IT 640281-90-9
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (treatment of Flaviviridae infection with 2'-branched nucleosides and another mutation-inducing drug such as interferon)
 RN 640281-90-9 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



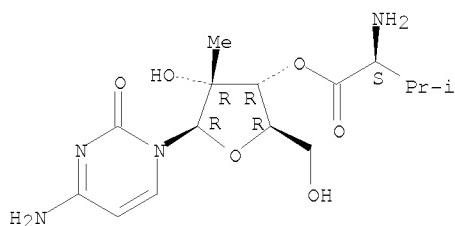
L11 ANSWER 35 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2004:20697 CAPLUS
 DN 140:87662
 TI 2'- and 3'-nucleoside prodrugs for treating Flaviviridae infections
 IN Sommadossi, Jean-pierre; La Colla, Paolo; Storer, Richard; Gosselin, Gilles
 PA Idenix (Cayman) Limited, Cayman I.; Centre National de la Recherche Scientifique; Universita Degli Studi di Cagliari
 SO PCT Int. Appl., 2498 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 4

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| PI WO 2004003000 | A2 | 20040108 | WO 2003-IB3901 | 20030627 |
| WO 2004003000 | A3 | 20041104 | | |
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| CA 2490200 | A1 | 20040108 | CA 2003-2490200 | 20030627 |
| AU 2003263412 | A1 | 20040119 | AU 2003-263412 | 20030627 |
| EP 1525209 | A2 | 20050427 | EP 2003-761749 | 20030627 |
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| CN | 1678621 | A | 20051005 | CN | 2003-820690 | 20030627 |
| JP | 2005537242 | T | 20051208 | JP | 2004-517162 | 20030627 |
| CN | 1761677 | A | 20060419 | CN | 2003-820501 | 20030627 |
| US | 20070087960 | A1 | 20070419 | US | 2003-608907 | 20030627 |
| BR | 2003012271 | A | 20071106 | BR | 2003-12271 | 20030627 |
| CN | 101172992 | A | 20080507 | CN | 2007-10193301 | 20030627 |
| CN | 101172993 | A | 20080507 | CN | 2007-10199501 | 20030627 |
| WO | 2005020884 | A2 | 20050310 | WO | 2004-US15395 | 20040514 |
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| US | 20070027065 | A1 | 20070201 | US | 2004-5468 | 20041206 |
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| US | 20070027066 | A1 | 20070201 | US | 2004-5470 | 20041206 |
| US | 20070032449 | A1 | 20070208 | US | 2004-5441 | 20041206 |
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| US | 7192936 | B2 | 20070320 | | | |
| US | 20070037735 | A1 | 20070215 | US | 2004-5442 | 20041206 |
| US | 20070042939 | A1 | 20070222 | US | 2004-5445 | 20041206 |
| US | 20070042991 | A1 | 20070222 | US | 2004-5447 | 20041206 |
| US | 7365057 | B2 | 20080429 | | | |
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| US | 20070042990 | A1 | 20070222 | US | 2004-5471 | 20041206 |
| US | 20070060503 | A1 | 20070315 | US | 2004-5440 | 20041206 |
| US | 20070060498 | A1 | 20070315 | US | 2004-5444 | 20041206 |
| US | 20070060504 | A1 | 20070315 | US | 2004-5446 | 20041206 |
| US | 20070060541 | A1 | 20070315 | US | 2004-5466 | 20041206 |
| US | 20070060505 | A1 | 20070315 | US | 2004-5472 | 20041206 |
| MX | 2004PA12779 | A | 20050819 | MX | 2004-PA12779 | 20041216 |
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| IN | 2005DN00341 | A | 20070202 | IN | 2005-DN341 | 20050128 |
| US | 20070275883 | A1 | 20071129 | US | 2006-516928 | 20060906 |
| PRAI | US 2002-392350P | P | 20020628 | | | |
| US | 2002-392351P | P | 20020628 | | | |
| US | 2003-466194P | P | 20030428 | | | |
| US | 2003-470949P | P | 20030514 | | | |
| CN | 2003-820501 | A3 | 20030627 | | | |
| CN | 2003-820701 | A3 | 20030627 | | | |
| US | 2003-607909 | A1 | 20030627 | | | |
| US | 2003-608907 | A1 | 20030627 | | | |
| US | 2003-609298 | A1 | 20030627 | | | |
| WO | 2003-IB3901 | W | 20030627 | | | |
| WO | 2004-US15395 | W | 20040514 | | | |
| OS | MARPAT 140:87662 | | | | | |
| AB | 2' And 3'-Prodrugs of 1'-, 2'-, 3'-, or 4'-branched β -D or β -L nucleosides, or their pharmaceutically acceptable salts and derivs., are described which are useful in the prevention and treatment of Flaviviridae infections and other related conditions. These modified nucleosides provide superior results against flaviviruses and pestiviruses, including hepatitis C virus and viruses generally that replicate through an RNA-dependent RNA reverse transcriptase. Comps., compns., methods and uses are provided for the treatment of Flaviviridae infection, including HCV infection, that include the administration of an effective amount of the prodrugs of the invention, or their pharmaceutically acceptable salts or derivs. These drugs may optionally be administered in combination or alternation with further antiviral agents to prevent or treat Flaviviridae infections and other related conditions. Preparation of compds. of the invention is included. | | | | | |
| IT | 640725-71-9P | | | | | |
| | RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic | | | | | |

preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (nucleoside prodrugs for treating Flaviviridae infections)
 RN 640725-71-9 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

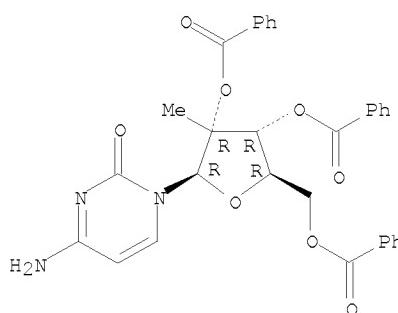
Absolute stereochemistry. Rotation (+).



● 2 HCl

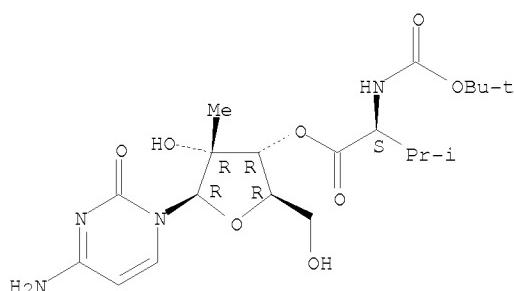
IT 640725-69-5P 640725-70-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (nucleoside prodrugs for treating Flaviviridae infections)
 RN 640725-69-5 CAPLUS
 CN Cytidine, 2'-C-methyl-, 2',3',5'-tribenzoate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 640725-70-8 CAPLUS
 CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with
 2'-C-methylcytidine (CA INDEX NAME)

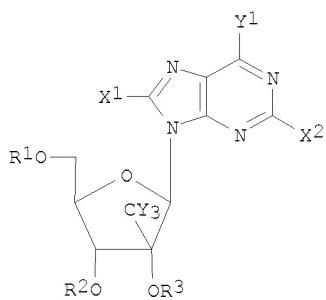
Absolute stereochemistry.



AN 2004:20696 CAPLUS
 DN 140:77365
 TI Preparation of modified 2'- and 3'-nucleoside prodrugs for treating Flaviviridae infections
 IN Sommadossi, Jean-pierre; La Colla, Poalo; Storer, Richard; Gosselin, Gilles
 PA Idenix (Cayman) Limited, Cayman I.; Universita degli studi di Cagliari; Centre National de la Recherche Scientifique
 SO PCT Int. Appl., 201 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 4

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|----------|
| PI WO 2004002999 | A2 | 20040108 | WO 2003-IB3246 | 20030627 |
| WO 2004002999 | A3 | 20040812 | | |
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| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2490191 | A1 | 20040108 | CA 2003-2490191 | 20030627 |
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| CN 1678621 | A | 20051005 | CN 2003-820690 | 20030627 |
| JP 2005533817 | T | 20051110 | JP 2004-517158 | 20030627 |
| CN 1761677 | A | 20060419 | CN 2003-820501 | 20030627 |
| US 20070087960 | A1 | 20070419 | US 2003-608907 | 20030627 |
| BR 2003012286 | A | 20070619 | BR 2003-12286 | 20030627 |
| CN 101172992 | A | 20080507 | CN 2007-10193301 | 20030627 |
| CN 101172993 | A | 20080507 | CN 2007-10199501 | 20030627 |
| WO 2005020884 | A2 | 20050310 | WO 2004-US15395 | 20040514 |
| WO 2005020884 | A3 | 20060622 | | |
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| US 20070027066 | A1 | 20070201 | US 2004-5470 | 20041206 |
| US 20070032449 | A1 | 20070208 | US 2004-5441 | 20041206 |
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| US 20070060498 | A1 | 20070315 | US 2004-5444 | 20041206 |
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| US 20070060505 | A1 | 20070315 | US 2004-5472 | 20041206 |
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| US 2003-470949P | P 20030514 | | |
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| CN 2003-820701 | A3 20030627 | | |
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| US 2003-608907 | A1 20030627 | | |
| US 2003-609298 | A1 20030627 | | |
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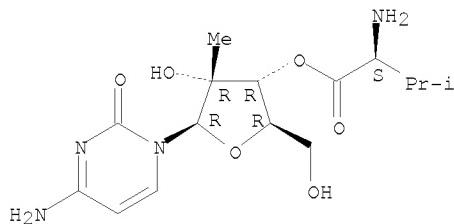


AB 2' And/or 3' prodrugs of 1', 2', 3' or 4'-branched-nucleosides I, wherein R1-R3 are independently H, phosphate, alkyl, acyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, CO-aryloxyalkyl, CO-substituted aryl, sulfonate ester, benzyl, wherein the Ph group is optionally substituted with one or more substituents, alkylsulfonyl, arylsulfonyl, aralkylsulfonyl, lipid, amino acid, carbohydrate, peptide, cholesterol; Y1 is hydrogen, bromo, chloro, fluoro, iodo, CN, OH, OR4, NH2, NHR4, NR4R5, SH or SR4; X1 and X2 are independently alkyl, CH3, CF3, CY3, 2-Br-Et, CH2F, CH2Cl, CH2CF3, CF2CF3, CY2CY3, CH2OH, alkenyl, alkynyl, COOH, COOR4, COO-alkyl, COO-aryl, CO-O-alkoxyalkyl, CONH2, CONHR4, CON(R4)2, halo, CN, N3, OH, CR4, NH2, NHR4, NR4R5, SH or SR5; Y is independently H, halo; and each R4 and R5 is independently hydrogen, acyl, alkyl, lower alkyl, alkenyl, alkynyl or cycloalkyl, and their pharmaceutically acceptable salts and derivs. are described. These prodrugs are useful in the prevention and treatment of Flaviviridae infections, including HCV infection, and other related conditions. Compds. and compns. of the prodrugs of the present invention are described. Methods and uses are also provided that include the administration of an effective amount of the prodrugs of the present invention, or their pharmaceutically acceptable salts or derivs. These drugs may optionally be administered in combination or alteration with further anti-viral agents to prevent or treat Flaviviridae infections and other related conditions. Thus, antiviral activity of β -D-2'-C-methyl-7-methyl-6-phenyl-3,3a,5,8a-tetrahydro-1,3,4,5,7a-penta-aza-s-indacen-8-one is reported.

IT 640281-90-9P
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of modified and nucleoside prodrugs for treating flaviviridae infections)

RN 640281-90-9 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L11 ANSWER 37 OF 37 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:20443 CAPLUS
DN 140:70984
TI 2'-C-methyl-3'-O-L-valine ester ribofuranosyl cytidine for treatment of flaviviridae infections
IN Sommadossi, Jean-Pierre; La Colla, Paolo
PA Idenix (Cayman) Limited, Cayman I.; Universita Degli Studi di Cagliari
SO PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| | CN 1678326 | A | 20051005 | CN 2003-820701 | 20030627 |
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| | BR 2003012278 | A | 20070619 | BR 2003-12278 | 20030627 |
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| US 20070042939 | A1 | 20070222 | US 2004-5445 | 20041206 |
| US 20070042991 | A1 | 20070222 | US 2004-5447 | 20041206 |
| US 7365057 | B2 | 20080429 | | |
| US 20070042940 | A1 | 20070222 | US 2004-5467 | 20041206 |
| US 20070042990 | A1 | 20070222 | US 2004-5471 | 20041206 |
| US 20070060503 | A1 | 20070315 | US 2004-5440 | 20041206 |
| US 20070060498 | A1 | 20070315 | US 2004-5444 | 20041206 |
| US 20070060504 | A1 | 20070315 | US 2004-5446 | 20041206 |
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| US 20070060505 | A1 | 20070315 | US 2004-5472 | 20041206 |
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| US 20070275883 | A1 | 20071129 | US 2006-516928 | 20060906 |
| IN 2007DN08806 | A | 20080111 | IN 2007-DN8806 | 20071115 |

PRAI US 2002-392351P
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 CN 2003-820501 A3
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 US 2003-608907 A1
 US 2003-609298 A1
 WO 2003-US20431 W
 WO 2004-US15395 W
 IN 2005-DN344 A3
 20050128

OS MARPAT 140:70984

AB The 3'-L-valine ester of β -D-2'-C-methyl-ribofuranosyl cytidine provides superior results against flaviviruses and pestiviruses, including hepatitis C virus. Based on this discovery, compds., compns., methods and uses are provided for the treatment of flaviviridae, including HCV, that include the administration of an effective amount of val-mCyd or its salt, ester, prodrug or derivative, optionally in a pharmaceutically acceptable carrier. In an alternative embodiment, val-mCyd is used to treat any virus that replicates through an RNA-dependent RNA polymerase. Several examples are provided of the pharmacol., mechanism of action, metabolism, side effects, and clin. efficacy of the title compound

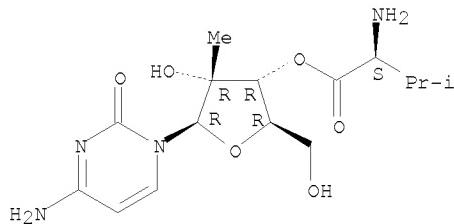
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 642075-77-2

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (ribofuranosylcytidine methylvaline ester combined with other antivirals for treatment of flaviviridae infections)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 642075-50-1 CAPLUS

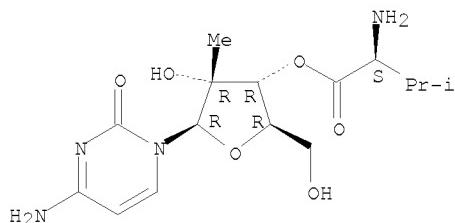
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 4-methylbenzenesulfonate (salt) (9CI) (CA INDEX NAME)

10/609, 298

CM 1

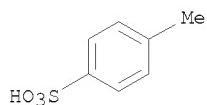
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 104-15-4
CMF C7 H8 O3 S

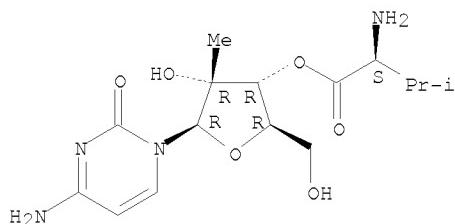


RN 642075-51-2 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, methanesulfonate (salt) (9CI)
(CA INDEX NAME)

CM 1

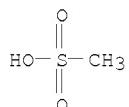
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 75-75-2
CMF C H4 O3 S



RN 642075-52-3 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, acetate (salt) (9CI) (CA

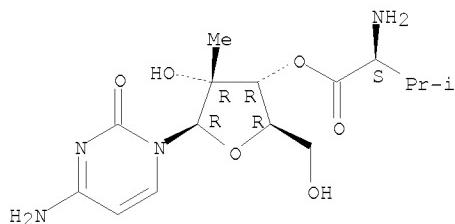
McIntosh

INDEX NAME)

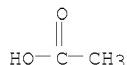
CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



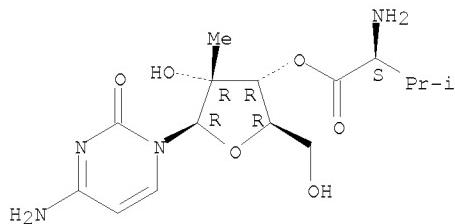
CM 2

CRN 64-19-7
CMF C2 H4 O2RN 642075-53-4 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-hydroxy-1,2,3-propanetricarboxylate (salt) (9CI) (CA INDEX NAME)

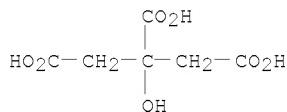
CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



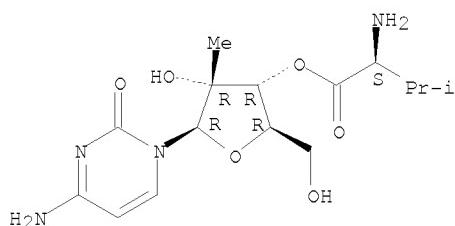
CM 2

CRN 77-92-9
CMF C6 H8 O7RN 642075-54-5 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, propanedioate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



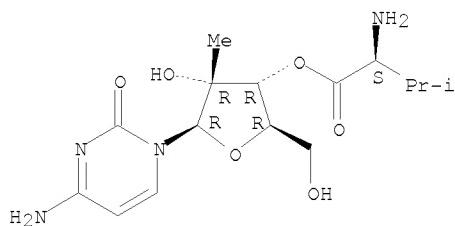
CM 2

CRN 141-82-2
CMF C3 H4 O4 $\text{HO}_2\text{C}-\text{CH}_2-\text{CO}_2\text{H}$ RN 642075-55-6 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, (2R,3R)-2,3-dihydroxybutanedioate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

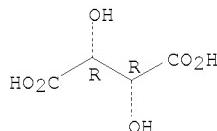
Absolute stereochemistry. Rotation (+).



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

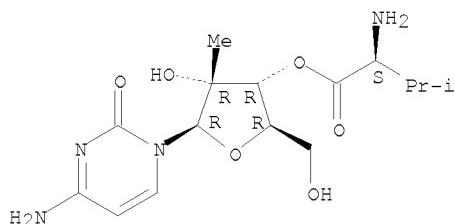
RN 642075-56-7 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, butanedioate (salt) (9CI) (CA INDEX NAME)

10/609, 298

CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-15-6
CMF C4 H6 O4

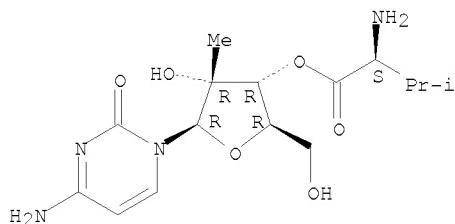
HO₂C—CH₂—CH₂—CO₂H

RN 642075-57-8 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, benzoate (salt) (9CI) (CA INDEX NAME)

CM 1

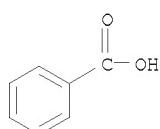
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 65-85-0
CMF C7 H6 O2



RN 642075-58-9 CAPLUS
CN L-Ascorbic acid, compd. with L-valine 3'-ester with 2'-C-methylcytidine (9CI) (CA INDEX NAME)

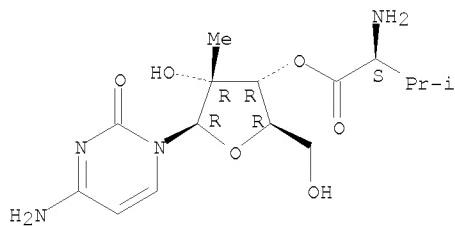
CM 1

McIntosh

10/609,298

CRN 640281-90-9
CMF C15 H24 N4 O6

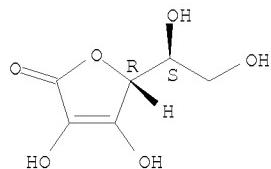
Absolute stereochemistry. Rotation (+).



CM 2

CRN 50-81-7
CMF C6 H8 O6

Absolute stereochemistry.

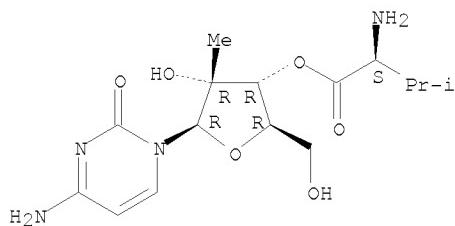


RN 642075-59-0 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-oxopentanedioate (salt)
(9CI) (CA INDEX NAME)

CM 1

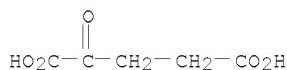
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CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 328-50-7
CMF C5 H6 O5



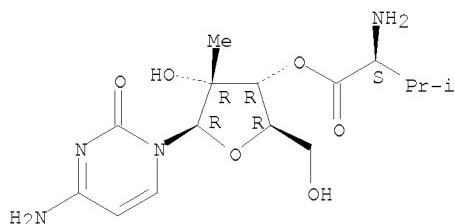
RN 642075-60-3 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2,3-dihydroxypropyl phosphate
(salt) (9CI) (CA INDEX NAME)

10/609,298

CM 1

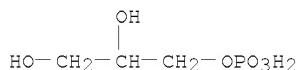
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 57-03-4
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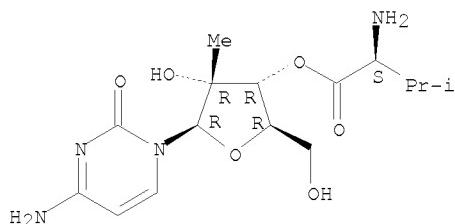


RN 642075-61-4 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, formate (salt) (9CI) (CA INDEX NAME)

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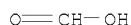
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 64-18-6
CMF C H2 O2



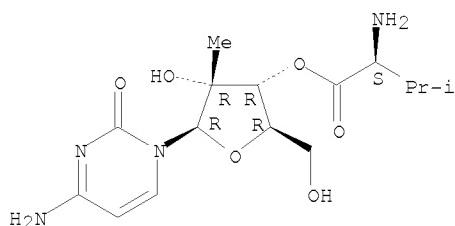
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CN L-Valine, 3'-ester with 2'-C-methylcytidine, (2E)-2-butenedioate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

McIntosh

Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

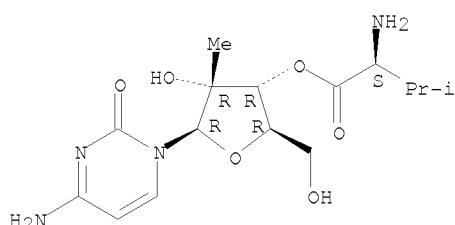


RN 642075-63-6 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, propanoate (salt) (9CI) (CA INDEX NAME)

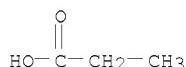
CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

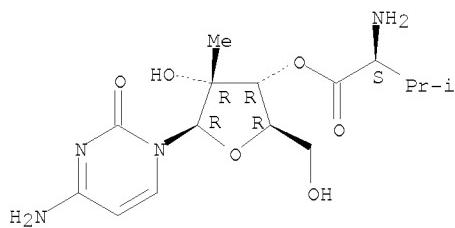
CRN 79-09-4
CMF C3 H6 O2

RN 642075-64-7 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydroxyacetate (salt) (9CI) (CA INDEX NAME)

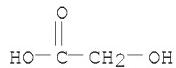
CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

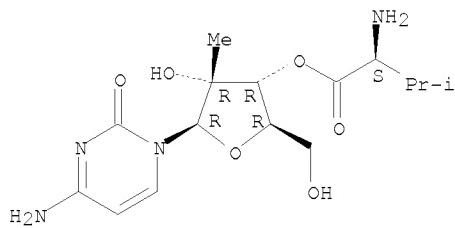
CRN 79-14-1
CMF C2 H4 O3

RN 642075-65-8 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-hydroxypropanoate (salt)
 (9CI) (CA INDEX NAME)

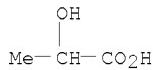
CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

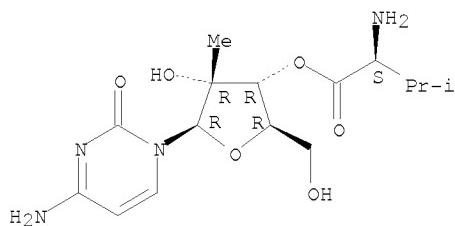
CRN 50-21-5
CMF C3 H6 O3

RN 642075-66-9 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-oxopropanoate (salt) (9CI)
 (CA INDEX NAME)

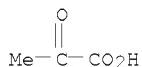
CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

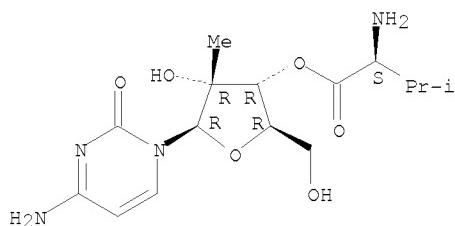
CRN 127-17-3
CMF C3 H4 O3

RN 642075-67-0 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, ethanedioate (salt) (9CI)
 (CA INDEX NAME)

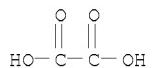
CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

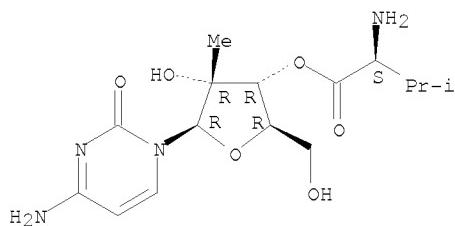
CRN 144-62-7
CMF C2 H2 O4

RN 642075-68-1 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, (2Z)-2-butenedioate (salt)
 (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

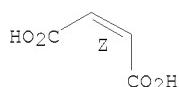
Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-16-7
CMF C4 H4 O4

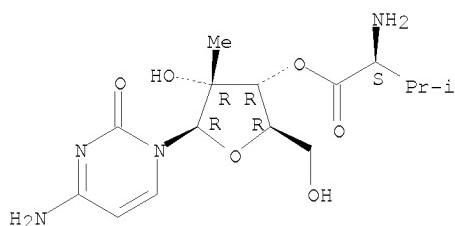
Double bond geometry as shown.

RN 642075-69-2 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-hydroxybenzoate (salt)
(9CI) (CA INDEX NAME)

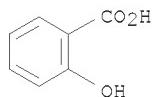
CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



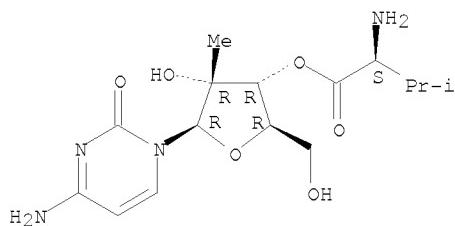
CM 2

CRN 69-72-7
CMF C7 H6 O3RN 642075-70-5 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, sulfate (salt) (9CI) (CA INDEX NAME)

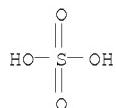
CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

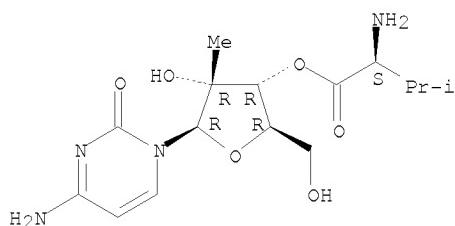
CRN 7664-93-9
CMF H2 O4 S

RN 642075-71-6 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, nitrate (salt) (9CI) (CA INDEX NAME)

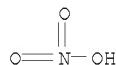
CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

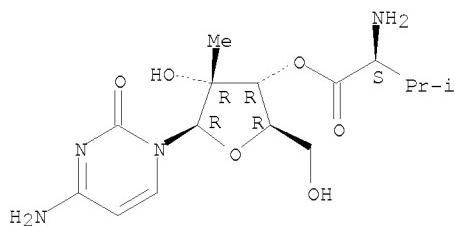
CRN 7697-37-2
CMF H N O3

RN 642075-72-7 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, carbonate (salt) (9CI) (CA INDEX NAME)

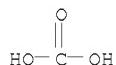
CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

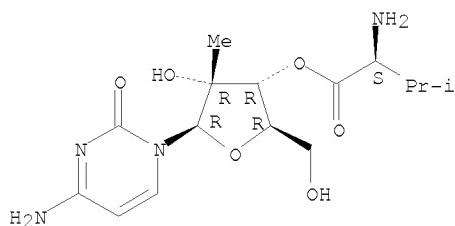
Absolute stereochemistry. Rotation (+).



CM 2

CRN 463-79-6
CMF C H2 O3RN 642075-74-9 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrobromide (9CI) (CA INDEX NAME)

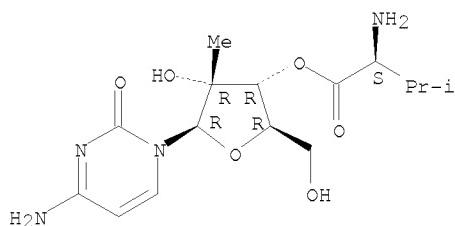
Absolute stereochemistry. Rotation (+).



● x HBr

RN 642075-75-0 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydriodide (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



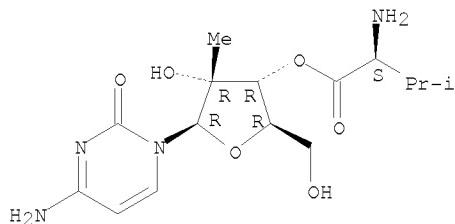
● x HI

RN 642075-76-1 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, carbonate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

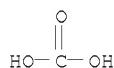
CRN 640281-90-9
 CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 463-79-6
 CMF C H2 O3

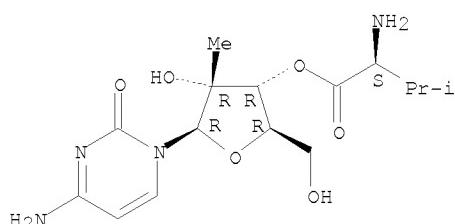


RN 642075-77-2 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, phosphate (salt) (9CI) (CA INDEX NAME)

CM 1

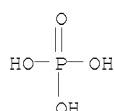
CRN 640281-90-9
 CMF C15 H24 N4 O6

Absolute stereochemistry. Rotation (+).



CM 2

CRN 7664-38-2
 CMF H3 O4 P

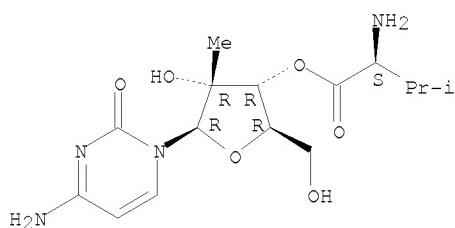


IT 640281-90-9P
 RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (ribofuranosylcytidine methylvaline ester for treatment of flaviviridae infections)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



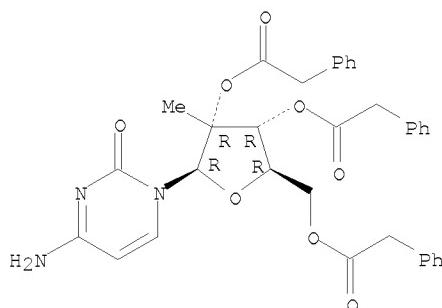
IT 642075-41-0

RL: RCT (Reactant); RACT (Reactant or reagent)
(ribofuranosylcytidine methylvaline ester for treatment of
flaviviridae infections)

RN 642075-41-0 CAPLUS

CN Cytidine, 2'-C-methyl-, 2',3',5'-tris(benzeneacetate) (9CI) (CA INDEX
NAME)

Absolute stereochemistry.



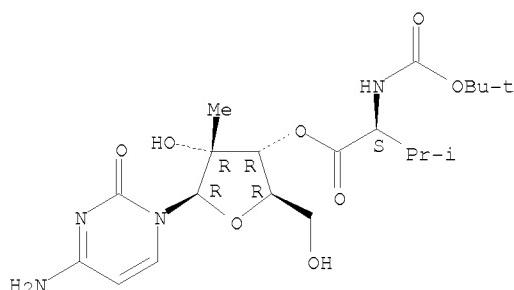
IT 640725-70-8P 642075-44-3P 642075-48-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(ribofuranosylcytidine methylvaline ester for treatment of
flaviviridae infections)

RN 640725-70-8 CAPLUS

CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with
2'-C-methylcytidine (CA INDEX NAME)

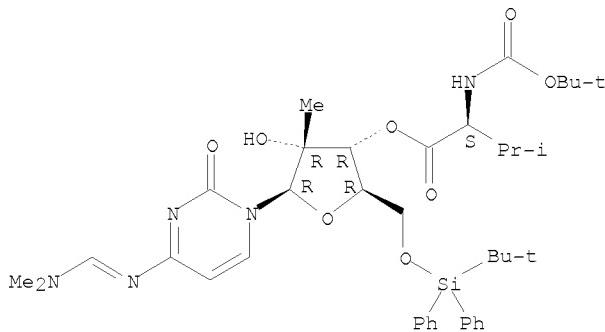
Absolute stereochemistry.



RN 642075-44-3 CAPLUS

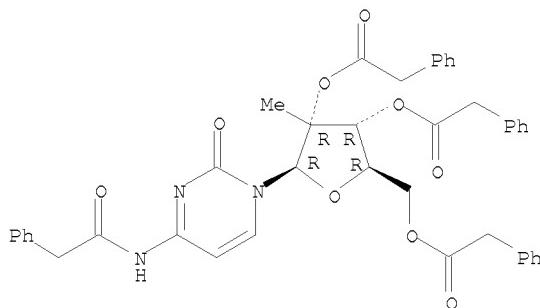
CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 3'-ester with
5'-O-[(1,1-dimethylethyl)diphenylsilyl]-N-[(dimethylamino)methylene]-2'-C-
methylcytidine (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



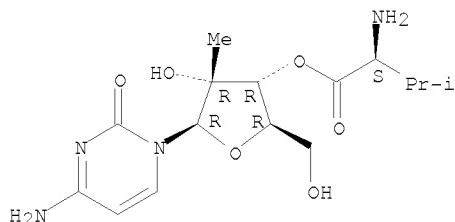
RN 642075-48-7 CAPLUS
 CN Cytidine, 2'-C-methyl-N-(phenylacetyl)-, 2',3',5'-tris(benzeneacetate)
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 640725-71-9P
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (ribofuranosylcytidine methylvaline ester for treatment of
 flaviviridae infections)
 RN 640725-71-9 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



●2 HCl

=> d his

10/609,298

(FILE 'HOME' ENTERED AT 18:07:49 ON 08 JUN 2008)

FILE 'REGISTRY' ENTERED AT 18:07:59 ON 08 JUN 2008
L1 STRUCTURE uploaded

L2 24 S L1
L3 519 S L1 FULL

FILE 'CAPLUS' ENTERED AT 18:08:46 ON 08 JUN 2008

L4 120 S L3
L5 22498 S L4 AND FLAVIVIRUS OR PESTIVIRUS OR FLAVIVIRIDAE OR HCV OR HEP
L6 58 S L4 AND (FLAVIVIRUS OR PESTIVIRUS OR FLAVIVIRIDAE OR HCV OR HE

FILE 'REGISTRY' ENTERED AT 18:13:47 ON 08 JUN 2008

L7 STRUCTURE uploaded
L8 4 S L7
L9 171 S L7 FULL

FILE 'CAPLUS' ENTERED AT 18:14:23 ON 08 JUN 2008

L10 74 S L9
L11 37 S L10 AND (FLAVIVIRUS OR PESTIVIRUS OR FLAVIVIRIDAE OR HCV OR H